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Studies on the Etiology of Goiter Including Graves' Disease.*

By David Marine, *New York*

IT is scarcely necessary to repeat to this audience the usual expression of feeling greatly honored at being invited to discuss certain features of my work in the University where I spent 15 pleasant years and where foundations of anything I have done in medicine were laid. It is necessary, however, out of fairness, to explain to this audience that much of the work I shall talk about tonight is the combined outcome of the friendly discussions, criticisms and hard work of men well honored and now living in Cleveland. I have particularly in mind the names of Lenhart, Stewart, Sollmann, Crile, Graham and Kimball.

Special interest in the problem of goiter was aroused the morning I arrived in Cleveland to join the resident staff of Lakeside Hospital. While walking from the Hollenden Hotel to the hospital, I saw several dogs with enlarged necks, three of which I stopped and examined. Since then my spare time has been spent working on one or another subject directly or indirectly connected with the goiter problem.

My curiosity was only that natural to a young medical graduate who had been suddenly transported from a region (Baltimore) where goiter was rare to a district where it was endemic. I quickly learned that my curiosity had been shared by other and more able medical men for the past 3000 years and that much of the knowledge which has now been established by painstaking investigation was suspected or known in a general way by the ancients.

The term goiter as now used is restricted to enlargement of the thyroid gland and is believed to have been derived from the Latin *guttur*, meaning throat. The first complete anatomical description of this gland was given by Thomas Wharton, the English anatomist, and published in 1659. He also gave it its present name. Every school child has a general idea of the size, location and outline of the thyroid sufficient to meet all practical needs and for our present purposes it is not necessary to review the anatomy in detail.

On the other hand, a general idea of the function of this important gland is absolutely essential for an understanding of the diseases with which it is more or less intimately associated. The

*McBride Lecture, Western Reserve University, delivered Nov. 11, 1929.

story of our present knowledge of thyroid function may be more impressively told in the form of a historical summary of the more outstanding facts.

Prior to 1874 some of the functions ascribed to the thyroid, that is, that it served to protect the vocal cords from cold, that it produced a secretion to moisten the larynx, that it gave form to the neck, that it served as a vascular shunt to control the brain circulation, were highly fanciful. In 1874 Sir William Gull published an account of a peculiar cachexia associated with atrophy of the thyroid. The outstanding clinical manifestations of this cachexia were loss of hair, drying of the skin, hard edematous thickening of the subcutaneous tissues, marked mental deterioration, extreme sensitiveness to cold and very great lessening of all bodily functions. Because of the peculiar changes in the skin and subcutaneous tissues, Sir William Ord in 1878 gave it the name "myxedema". The observation of Gull, therefore, marks the beginning of our real knowledge of thyroid physiology.

In 1882 the Reverdin brothers published a brief report and in 1883 Theodore Kocher published a much more complete account of the effects of complete removal of large goiters in human beings.

Most of the patients upon whom this operation was performed developed what we now recognize as parathyroid tetany but a few developed a symptom-complex (cachexia strumapriva) which Kocher recognized as being essentially identical with that described by Gull nine years earlier. This condition was soon produced at will in many species of animals by the removal of the thyroid.

In 1891 Murray reported the cure of a case of Gull's disease by injecting a glycerol extract of fresh sheep's thyroid and about the same time in Germany it was observed that feeding the gland by mouth, either fresh or dried, produced the same effect.

In 1895 Magnus-Levy, using the newly developed calorimeter, found that the essential effect of feeding thyroid gland substance either to individuals with myxedema or to normal persons was to raise their total metabolism, that is, it greatly increased their oxygen consumption and heat production and up to the present time this acceleration of oxidation processes is the only known physiological and pharmacological effect of the thyroid.

Also in 1895 Baumann of Freiburg discovered the presence of iodine as a normal constituent of the gland and Oswald of Zurich in 1899 showed that the iodine was contained mainly in the colloid material and firmly bound with the globulin fraction as an iodothyroglobulin.

The work done in this university between 1905 and 1910 by Williams, Lenhart and myself showed that the iodine store was intimately related to the structure and the function of the thyroid gland. It was demonstrated that the essential change in the development of goiter was a tremendous decrease in the iodine store in the gland and that this held true for all the species of animals examined. It was further shown that the administration of iodine caused a very rapid storage of this substance in the gland and brought about the involu-

tion of any existing hyperplasia as well as preventing any possible development of hyperplasia.

In 1916 Kendall of the Mayo Clinic reported the isolation of a crystalline substance from the thyroid containing about 65% of iodine which he named thyroxin and which was found to have effects on metabolism similar to those observed by Magnus-Levy in 1895 following the administration of the whole gland substance. Kendall attempted to determine the structure of thyroxin but failed. In 1926 Harington and Barger in a brilliant research perfected a simple method of isolating the substance in larger amounts, succeeded in determining its chemical structure and in the following year made it synthetically.

Whether thyroxin is the only active principle of the thyroid is not known, but it certainly accounts for its chief and only known function. To summarize: The major function of the thyroid is to provide the means through its iodine containing hormone, thyroxin, for maintaining a higher rate of metabolism or oxidation processes than would otherwise exist and also through fluctuations in activity it provides a means for varying the rate of metabolism to meet changing physiological needs.

Another important phase of thyroid function deals with its interrelations with other glands, as for example, the pituitary gland, the suprarenals, the ovaries, the testes and thymus. Our knowledge of these interrelations is still very meagre and a general summary would not be very helpful here. However, certain of these interrelations will be briefly referred to in the discussion of thyroid diseases.

The important diseases of the thyroid associated with disturbances of its functions may be divided into two general groups as follows:

Group I. Thyroid insufficiencies (hypothyroidism)
1. Simple or endemic goiter
2. Myxedema
   a. of infants (cretinism)
   b. of adults (Gull's disease)

Group II. Graves' disease (hyperthyroidism)

As I shall say only a few words regarding Graves' disease, it will be better to dispose of this before going on with the main topic of this lecture.

Graves' disease is a serious disease, easily recognizable and characterized by a chronic afebrile increase in metabolism and heart rate, marked general weakness, a highly nervous state and less frequently by protrusion of the eyes and thyroid enlargement. The incidence is rapidly increasing in all industrialized countries and concerning its nature very little that is definite is known. The view that it is essentially a thyroid disease is still the pervailing one but I am convinced that the primary and fundamental disturbance lies elsewhere—probably in a deficiency of some function of the suprarenal cortex and sex glands, which has to do with the regulatory control of oxidation processes in the various tissues. Graves' disease is clearly a loss of control of these oxidation processes and as a result of this there is an excessive

production by the thyroid of its very powerful activator of oxidation, thyroxin.

Three facts of importance have been discovered during the last ten years bearing directly on the etiology. The first is that a symptom complex closely resembling Graves' disease can be produced in a large percentage of rabbits and cats by sufficient injury of the suprarenal glands. The outstanding symptoms of Graves' disease which can thus be produced experimentally are increased metabolism, myasthenia, regeneration of the thymus and lymph glands, increased appetite, a change in temperament, increased irritability and hypersusceptibility to drugs. The conclusion that the symptom-complex which follows sufficient injury of the suprarenals is closely related to Graves' disease is not generally accepted but it cannot be ignored even though it is only a very crude reproduction, or glimpse of the natural disease. One obvious reason for this crudeness is that the suprarenal gland is at least a dual gland whose functions are to some extent antagonistic and in injuring the cortical portion we of necessity seriously cripple the medulla, or epinephrine secreting tissue, while in Graves' disease this is not the case. As is well known, epinephrine is the most rapid activator of metabolism known.

The second fact deals with the attempts to obtain a physiologically active substance from the suprarenal cortex that would lower or regulate thyroid activity. A great number of extracts have been studied by various workers, notably Stewart and Rogoff in this university, but I can here mention only those that appear to have a bearing on Graves' disease. During the last ten years we have consistently observed that glycerol extracts of fresh ox suprarenal cortex when fed to cases of Graves' disease regularly caused an outstanding gain in weight, a gain in muscle strength and gradual lowering of the metabolism. Attempts to concentrate this substance always ended in failure. On this account we were never able to obtain more than a glimpse of its activity and the impression that it was unstable in air.

The third fact is the discovery reported last year by Szent-Gyorgyi. He isolated from the suprarenal cortex an active reducing substance in crystalline form, which is unstable and readily destroyed in the presence of atmospheric oxygen and which he thought was a hexuronic acid. The work which we have so far done with this substance would indicate that it has very striking effects on the oxidation and reduction processes going on in the living tissues and particularly that it lowers the activity of the thyroid gland, as indicated by the fact that it causes thyroid involution.

These three facts—first, the experimental production of a Graves' disease-like symptom-complex in animals, second, the slight but obvious beneficial therapeutic effect of cortical extracts administered by mouth to cases of Graves' disease and third, the isolation of a highly unstable hexuronic acid from the cortex which involutes thyroid hyperplasia—I believe mark a definite advance toward the solution of Graves' disease by establishing with certainty that some internal secretion of the suprarenal cortex and sex

glands play an important role in regulating tissue oxidations, particularly when considered in association with the long known fact that the most outstanding physiological abnormality in Graves' disease is a derangement of the regulatory control of tissue oxidations.

After this digression we can turn to the main subject of this talk, namely, thyroid insufficiencies of which simple or endemic goiter, cretinism and myxedema are the three outstanding clinical associations. So far as is known, the great medical character of the middle ages, Paracelsus, was the first to point out the close relationship between endemic goiter and cretinism. All subsequent study has strengthened this association and firmly established the view that they are but different stages or degrees of the same nutritional fault. This idea was first forcibly expressed by Morel in his famous dictum, "Goiter is the first step on the road to cretinism", and later by Koestl, that the condition which produced goiter when it is weak also produces cretinism when it is intense.

As endemic cretinism in man does not occur in America I shall limit the discussion to simple or endemic goiter.

Occurrence and Distribution

Simple goiter includes those thyroid enlargements in man and animals which were formerly grouped under endemic, epidemic, sporadic and physiologic. It may occur in any land and fresh water animal with the ductless thyroid. Animals living in the sea are free from the disease. On the seacoast generally it is ordinarily rare in man and the cases seen are usually in women and in association with pregnancy and lactation. It occurs in all races, in all climates and at all inhabitable altitudes. In the temperate zones there is a seasonable variation, both in man and animals. It develops more frequently during the late winter and early spring months. Similar seasonal variations also occur in the iodine store of the thyroid as pointed out by Seidell and Fenger. While goiter may occur anywhere, even in mid-ocean, as on one of Capt. Cook's voyages in 1772, one of the most striking characteristics is the increased incidence in certain more or less defined regions of the world, in so-called districts of endemic goiter (Hirsch). The most notable of these districts are the Himalaya Mountain region of South Central Asia, the Alps, Pyrenees and Carpathian Mountain regions in Europe, the Andean plateau of South America. In North America the most important areas are the St. Lawrence River and Great Lakes basin, extending west through Minnesota, the Dakotas and the adjacent Canadian provinces and also the Pacific Northwest, including Oregon, Washington and British Columbia. Less important foci occur throughout the Appalachian Mountain region, the Rocky Mountain states and states in the Great Central Basin. It will be noted that most of these regions are mountainous, although there are numerous exceptions. Of greater importance is the occurrence of endemic goiter for the most part on soils deposited from the last glacial period.

There is also general evidence of variations in the incidence of goiter in these districts during the last 100 years. There are many reports of the

sudden occurrence of large numbers of goiters, the so-called epidemics, both in man and animals. In man these so-called epidemics have for the most part occurred in military garrisons, in institutions and in schools. These outbreaks have usually been in districts where the ordinary incidence of goiter is high and in newly arrived people. I have had opportunity of investigating such outbreaks in dairy herds, on poultry farms and in fish hatcheries. Some of these outbreaks were in goiter regions while others were not, showing that with the optimum conditions for its development present, goiter may occur anywhere.

Beginning about the age of puberty, females are more often affected than males. In the districts of severest endemic goiter this difference in incidence due to sex is masked. In such regions all of the inhabitants may be affected. In non-goiter regions where only sporadic cases occur these are usually seen in women. Striking an average between these two extremes one may say that in general simple goiter is two or three times more common in females. In the lower animals a difference in incidence due to sex has not been demonstrated. The periods in life when simple goiter most frequently develops are (a) during fetal life, (b) during pregnancy and lactation, (c) during puberty and (d) during the menopause.

Etiology

Despite the fact that the cause of endemic goiter has been sought since the earliest days of medicine, the fundamental cause is still unknown. A great variety of agents have been brought forward from time to time as casual factors.

In 1867 St. Lager grouped the various causal factors under forty headings, most of which now have only a folklore or legendary interest. Certain of them, as for example water, poverty, damp sunless habitations and especially diet, are of general importance today. A great variety of mineral constituents of soil and water, as for example salts of calcium and magnesium, sulphides, particularly of iron, fluorides and silica, were at one time suspected. With the development of bacteriology and protozoology the view that goiter might be due to a specific living virus was widely adopted and is still held by some. Many types of organism, bacteria, fungi and protozoa, have been described. McCarrison thought that a member of the colon group of bacteria was the cause. Chagas thought a trypanosome caused endemic goiter in Brazil and numerous reports have appeared suggesting organisms of the diphtheroid group.

Despite this enormous amount of work nothing suggesting a direct infecting agent has been proven. That bacterial toxins may indirectly stimulate the thyroid to enlargement is well known, as for example pulmonary tuberculosis, syphilis and pneumonia. Water has been asociated as a carrier of the goiter producing agent by all peoples from the remotest times. Livingstone reported that the inhabitants of Central Africa held this belief. Barton, in 1800, stated that the Indians inhabitating the shores of Lakes Ontario and Erie thought that water which contained soluble products of decomposing leaves and other vege-

table matter was responsible since goiter was more common in the fall and winter months. The Romans were convinced that snow water was a cause. Water certainly is a factor in the etiology of goiter and the conflicting data in the light of our present knowledge could be best correlated by assuming a deficiency of some substance (iodine) which is necessary for the prevention of goiter rather than that water contains some virus or toxin capable of inducing goiter.

The present view of the cause of simple goiter assumes that it is a work or compensatory hypertrophy of the thyroid depending immediately upon a relative or absolute deficiency of iodine.

This leaves the ultimate or fundamental causes of iodine deficiency still to be determined but concerning which very important contributions have recently been made, to which I shall presently refer.

It is conceivable that the deficiency of iodine may be due to, first, factors which bring about an abnormally low intake of iodine, second, to factors which interfere with the absorption or utilization of an otherwise normal intake, or third, factors which temporarily or periodically increase the needs of the body for thyroxin, that is, factors which create a relative insufficiency of iodine. These three groups may be examined further.

Group 1—Factors bringing about an abnormally low iodine intake. This would partially explain the occurrence of endemic goiter. It is a simple, easily understandable conception and compatible with all the facts so far as it goes, but unfortunately the problem of goiter is much more complicated. The idea that goiter is due to a low iodine intake is not new. As early as 1830, that is within 19 years of the discovery of iodine as an element, such views were expressed. To be sure, a low chlorine intake was also advanced as the cause but this should have supported instead of detracting from the idea of the iodine deficiency since these two elements are so closely associated in nature.

The work of Chatin published in 1852 deserves special mention. He showed that there was a low iodine content in soil and water in districts of endemic goiter. His results were attacked and unfortunately so discredited on the ground of faulty technique and inadequate methods that further study of this important lead was blocked for 45 years, that is, until Baumann discovered iodine as a normal constituent of the thyroid in 1895. During the past 20 years very extensive analyses of foods, soils and water for iodine, particularly by McGlendon and Remington in this country and by von Fellenberg in Europe, have been made and all confirm Chatin's original claim.

Group 2—We have no information at present in regard to factors which interfere with the absorption or utilization of iodine in the body. It is conceivable that intestinal bacteria or various parasites could utilize or divert the iodine intake or that inherited or acquired defects in metabolism could prevent the thyroid gland from utilizing iodine but the evidence is entirely against any influence by these factors. Indeed, in all the vast experience now available no one has seen anything which suggests that the thy-

roid gland is unable to make thyroxin in a few hours after iodine is administered.

Group 3—Factors which temporarily or periodically increase the need of the organism for thyroxin. This group is more difficult to define or understand and from evidence now available it is by far the most important. There are many factors which are known to temporarily increase the needs of the organism for thyroxin, that is, factors which create a relative iodine insufficiency. Among the more important may be mentioned, *food, pregnancy, infectious diseases, puberty* and *Graves' disease*. As already mentioned, food has long been known to influence the thyroid. St. Lager mentions that the Alpine people thought that eating large quantities of pork fat caused thyroid enlargement. Baumann observed that diets consisting entirely of meat caused a reduction in the iodine store of dogs' thyroids. The work of Lenhart and myself on goiter in brook trout demonstrated that a diet of pigs' liver was the major cause. Our observations in dairy herds showed that extensive feeding of oil cake often led to goiter in cattle.

About two years ago Chesney and Webster in Johns Hopkins University found that rabbits fed mainly with fresh cabbage developed goiter in from two to three months. This observation gave us a cheap, simple and practical method of producing goiter in the most practical of all laboratory animals. Taking up this work with my colleague, Dr. Emil J. Baumann, we quickly found that by steaming the cabbage for thirty minutes, goiter could be produced in seven to nine days instead of the two or three months required when fresh cabbage was fed. We further found that the cabbage cake from which 60% of its weight had been expressed as press juice was even more potent than the whole cabbage. We further observed that whereas hashed steamed cabbage was as potent as unhashed cabbage, hashed fresh cabbage lost most of its goiter producing quality. From these data we concluded that the goiter producing substance could be destroyed quickly by enzymes although it was heat stable and resisted oxidation in the air. We further observed that there was a very great seasonal or climatic variation in the goiter producing quality of cabbage. So-called summer cabbage was practically inert; whereas cabbage maturing late in the autumn, so-called winter cabbage, was usually extremely potent. All these observations indicated that we were dealing with at least two factors, (1) a goitrogenic and (2) an anti-goitrogenic, both of which show quantitative variations. The discovery last year by Szent-Gyorgyi helped us greatly at this point. As already mentioned, he isolated from cabbage, oranges and suprarenal cortex a very powerful auto-oxidizable substance. We have injected concentrates of this substance into rabbits and found that it was strongly anti-goitrogenic. It was now definite that in cabbage there exists two substances—one, a stable, powerfully goitrogenic substance occurring mainly in winter cabbage and the other, a very unstable, powerfully anti-goitrogenic substance occurring in greatest concentration in summer cab-

bage. Iodine is also antigoitrogenic but acts quite differently from the hexuronic acid. Iodine prevents goiter by supplying the necessary element from which the thyroid can readily make thyroxin while hexuronic acid appears to act by providing another means of augmenting tissue oxidations and in this way relieving or sparing the thyroid.

The goitrogenic substance has not yet been isolated. We know that it exists in many other members of the cabbage family and that it shows great seasonal variation. As above mentioned, a good cabbage will produce a palpable goiter in the rabbit in seven days. The development of the goiter is accompanied by a fall in metabolism, as shown by Webster and Chesney, which may be as rapid and as marked as that following thyroidectomy. Traces of iodine of course abolish entirely this effect of cabbage as it does with all other known goiter producing agents. The mode of action of the goitrogenic factor is apparently by depressing tissue oxidations and it would seem, therefore, that the thyroid enlargement is the result of an attempt on the part of the thyroid to overcome this depression.

We can now better understand the well known seasonal incidence of goiter, that is, in addition to a possible increase in the iodine intake during the summer months there is a greatly increased supply of the anti-goitrogenic substance from fresh growing plants which lessens the need for thyroid activity.

If this normal constituent of the suprarenal cortex and sex glands is antigoitrogenic, as all the evidence now available seems to indicate, then we have the further insight into the influence of sex, puberty, pregnancy and the menopause on the development of goiter, and, as already indicated, we have also made a beginning in the solution of Graves' disease. We now have something tangible regarding the nature of one of the factors which bring about the *relative* iodine deficiencies and subsequent thyroid enlargment in contradistinction to the thyroid enlargements dependent upon an *absolute* iodine deficiency.

To summarize:

Thyroid enlargement or goiter is apparently always due to a deficiency of iodine in the gland.

On the other hand this deficiency may be primary or absolute as first suggested by the work of Chatin in 1850 and this would explain the increased incidence of goiter in relation to certain regions of the world.

On the other hand the iodine deficiency may be secondary or relative, that is, the iodine intake may be normal, but owing to increased demands it is utilized so rapidly that it cannot be held in the thyroid in sufficient concentration to keep the gland from enlarging. This condition may be readily produced in brook trout by feeding liver, in white mice by feeding cracker meal and in rabbits and rats by feeding cabbage or other Brassicae. In the case of cabbage this relative iodine insufficiency is apparently produced by a powerful inhibitor of tissue oxidation. Also a relative iodine deficiency may be brought about by a deficiency of certain anti-goitrogenic biological oxidation systems of the type of glutathione and hexuuronic acid

Both of these substances are normally present in great concentration if not actually produced in the suprarenal cortex and sex glands. Stated more briefly, relative iodine deficiency goiter may be produced in rabbits either by cabbage with a high goitrogenic factor or a low antigoitrogenic factor.

These active oxidizing agents probably prevent thyroid enlargement indirectly by relieving the thyroid of excessive activity in bringing about biological oxidations, that is, a thyroid sparing action.

Iodine on the other hand is a direct anti-goitrogenic substance in that it is the essential constituent of the thyroid hormone and therefore prevents goiter by making it easier for the thyroid to produce an abundance of thyroxin.

Goiter due to a primary or absolute deficiency of iodine is definite and easily understood, whereas goiter due to a relative or secondary iodine deficiency is more difficult to define, less understood and by far the most important since no animal with the ductless thyroid is free from the possible influence of *diet, pregnancy, puberty,* and *infections.* These conditions are as active in regions where there is a real iodine deficiency, that is, in regions of endemic goiter, as in non-goitrous regions and when thus combined the effects of *diet, puberty, pregnancy, menopause* and *infection* are greatly increased. So much emphasis has been laid on iodine deficiency in the etiology of goiter that there is a tendency to forget to bear in mind that the deficiency of iodine may be secondary as well as primary.

The Relation of Experimental Rheumatoid Inflammation to Allergy*†

By B. J. Clawson, M.D., *Minneapolis, Minn.*

THE microscopic lesions found in acute rheumatic fever have quite generally come to be considered characteristic (not specific) anatomic features of the disease both by those who believe the streptococcus to be the exciting agent and by those who believe that the disease is produced by an unknown virus. The lesions show mononuclear and multinucleated cells with vesicular or hyperchromatic nuclei (the so-called Aschoff cells), lymphocytes, plasma cells, eosinophiles, and a varying number of polymorphonuclear leucocytes.

Such inflammation, either in nodules or in irregular diffuse arrangement, has been described as occurring in the subcutaneous tissues, joints, tendons, galea aponeurotica, diaphragm, tongue and other muscles, tonsils, arteries, and in the valves, auricles, and ventricles of the heart.

The lesions in the myocardium as described by Aschoff[1] and Geipel[2] were interstitial submiliary bodies composed of large mononuclear or multinucleated cells with vesicular nuclei. The cytoplasm of these cells stained red with methyl-green pyronin. There were lymphocytes, plasma cells in varying numbers, and occasionally polymorphonuclear leucocytes in the nodules.

The subcutaneous rheumatic nodules are localized areas of inflammation, mostly polyblastic in character, found in the loose connective tissue beneath the skin in some cases of acute rheumatic fever. The nodules have been studied microscopically by Hirschsprung,[3] Barlow and Warner,[4] Futcher,[5] Frank,[6] Swift,[7] and others. There is a general agreement by these observers that the subcutaneous nodules consist of proliferating connective tissue cells and a cellular exudate of lymphocytes, plasma cells, polymorphonuclear leucocytes, and that in the center of most of the nodules there is a greater or less amount of a homogeneous substance consisting of necrotic material and fibrin. It is also agreed that anatomically and etiologically the subcutaneous nodules are similar to the nodules in the heart described by Aschoff, Geipel, and Coombs,[8] and to the type of inflammation found in other parts of the body in acute rheumatic fever.

This type of inflammation whether found in the myocardium, subcutaneous tissues, or any other part of the body has come to be considered by

From the Department of Pathology, University of Minnesota.

*Read before the American College of Physicians, February 12, 1930.

many observers a specific reaction to the rheumatic virus. Others look upon these lesions as a polyblastic type of reaction common in rheumatic inflammation but not necessarily specific for the disease.

The first attempt to produce rheumatoid lesions experimentally was made in 1909 by Coombs, Miller, and Kettle[9]. They injected rabbits intravenously with streptococci isolated from the blood of patients with rheumatic infection and produced arthritis and myocardial lesions. Many of the lesions in the heart were nodular in form and showed the polyblastic type of reaction found in human rheumatic nodules in the myocardium. These authors decided that the difference existing between the experimental nodular infection and the human variety could be accounted for by the mode of entrance of the infectious agent in the two conditions.

Jackson[10] produced lesions in the interstitial tissues of the heart by injecting streptococci intravenously into rabbits. These nodular lesions were composed chiefly of large, irregular, mononuclear, and multinucleated ceils which did not differ from those found in the heart in rheumatic cases.

Areas of polyblastic inflammation mostly perivascular in arrangement were observed by Small[11] in a papule developing at the site of an intradermal injection of a streptococcic vaccine.

By injecting streptococci, previously agglutinated, into the left ventricular cavity of rabbits I[12] was able to produce nodular polyblastic lesions in the myocardium in 21 cases out of 34. Microscopically these lesions showed many multinucleated cells the cytoplasm of which stained red with methyl-green pyronin. Subcutaneous nodules[13] were also produced in a high percentage of cases by injecting strains of streptococci of low virulence in varying amounts at different intervals. With the larger doses abscesses developed. Morphologically the cells found in the smaller nodules were similar to those in human subcutaneous nodules and in human Aschoff nodules in the heart. It is evident that by injecting streptococci into the myocardium and the subcutaneous tissues of rabbits, lesions can be produced which morphologically show a marked similarity to the nodules found in the myocardium and subcutaneous tissues in cases of acute rheumatic fever.

Most of the animals used in the above experiments had been previously injected either intraarterially through the left ventricle of the heart or subcutaneously in one area with a mixture of streptococci and agar. Therefore, it could not be stated definitely whether the reaction in the nodules was influenced by existing immune or allergic reactions.

The phenomenon of allergy as related to rheumatic inflammation came into recent prominence through Swift's[14] work in a study of the hypersensitive (hyperergic) state of rabbits to streptococci, and a similar hypersensitiveness in people having acute rheumatic fever. Birkhaug[15] by skin tests also found that a high percentage of people having acute rheumatic fever were hypersensitive to streptococcic protein.

The following experiments were carried on in an attempt to determine

what part, if any, allergy or immunity played in the pathogenesis of the experimental rheumatoid lesions. If it is proved that animals hypersensitive to a bacterial protein, will respond to doses too small to call forth any reaction in nonsensitive animals and will react with the same type of cellular reaction which is produced by larger doses in non-sensitive animals, this may help to explain why in rheumatic patients who have been found to be hypersensitive to streptococci such extreme reactions take place when obviously very few organisms are present in the blood, joints, heart, etc.

The experimental lesions were produced by injecting streptococci (a rheumatic strain) in many places into the subcutaneous tissues of rabbits. One hundredth of a suspension of organisms in salt solution was injected into each of 10 places in the subcutaneous tissues in the backs of all animals on the right side and 1/1000 of a suspension was injected in a similar manner on the left side. The animals were killed 5 days after the multiple injections were made and the subcutaneous nodules, if present, were studied by gross and microscopic examination.

The following 3 groups were used in these experiments: (1) animals which had not been injected (normal animals); (2) animals which had been injected intravenously with streptococci (immune animals); (3) animals which had been injected subcutaneously in one area with agar at 45° C. heavily seeded with streptococci.

The occurrence of an inflammatory reaction was slight in the 10 normal animals (Table 1). At least 10 injections were made on each side. Nodules were present with the larger doses in 7 of the 10 animals, but the number of nodules compared with the number of injections was small. Fourteen nodules out of a possibility of 100 (14 per cent) were present on the side injected with the larger dose and only 3 out of a possibility of 100 (3 per cent) on the side which was injected with the smaller dose. All of these nodules were small in size except in one case where the 3 nodules were of medium size. In only one of the 10 animals were there any nodules on the side injected with the smaller doses and these nodules were very small.

By microscopic examination the reaction in the smaller nodules was polyblastic in character similar to that in Aschoff nodules and subcutaneous rheumatic nodules in human cases. In the few larger nodules abscess formation was found in the center but a considerable degree of polyblastic reaction was always present in the periphery of the nodules.

Agglutinins were not present in any of the animals at the time of the multiple injections (Table 1). Five of the 10 rabbits showed agglutinins in dilutions not higher than 1:200 in the blood 5 days after the multiple subcutaneous injections. A titer of 1:200, as will be seen later in a study of the immune animals, was very low. No apparent relation existed between the presence of agglutinins and the number, size, or character of the nodules in the normal animals.

The animals in the second group (immune animals) had been immunized by an intravenous injection of streptococci. Multiple injections were

then made subcutaneously with the larger and smaller doses into the tissues of the backs of the different animals at intervals of 1, 2, 3, 4, 5, 6, 7, 8, 10, and 12 days. Little reaction occurred in this group as indicated by frequency, size, and character of the subcutaneous nodules in the 12 animals which had received the multiple subcutaneous injections in from 1-5 days after the primary intravenous immunizing dose. Nodules were present in 3 of the 12 animals. Only 4 nodules were seen out of a possible 120 (3 per cent) on the side injected with the larger dose. No nodules were present on the left side in which the smaller doses were injected (Table 1). The nodules were small and firm and by microscopic examination showed a polyblastic inflammation similar to that in the small nodules in the normal animals (Fig. 1). It was evident that these 12 animals were not only not hypersensitive but that they had some degree of resistance since the number and size of the nodules were less than those found in the normal animals.

In the 11 animals which had the multiple subcutaneous injections in from 6-12 days after the primary inoculation there was a marked reaction. Nodules were present in 44 per cent of the injections with the larger doses and in 15 per cent of the injections with the smaller doses. The nodules were more frequent, larger, and sometimes were found on the side of the animal injected with the smaller doses. The microscopic reaction in the nodules differed in no way qualitatively from that found in the normal animals.

Two factors may be thought of as the cause of the quantitative difference in the reaction in the 2 divisions in group 2: (1) the time of multiple subcutaneous injections after the primary immunizing inoculation, and (2) the degree of concentration of the immune bodies in the blood of the animals. In the first division the time was from 1-5 days and in the second from

TABLE 1. RELATION OF EXPERIMENTAL SUBCUTANEOUS NODULES IN NORMAL, IMMUNE, AND ALLERGIC ANIMALS TO THE AGGLUTINATING TITER OF THE SERUM OF THE ANIMALS.

Kinds of Animals	No.	Percentage of Subcutaneous Injections Producing Nodules		Maximum Agglutinating Titer	
		Right Side with Larger Doses	Left Side with Smaller Doses	At Time of Multiple Injections	When Animals Were Killed
Normal	10	14	3	0	1:200
Immune A	12	3	0	1:200	1:6400+
Immune B	11	44	15	1:6400	1:6400+
Hyperimmune	8	9	2	1:256,000	1:300,000
Allergic	12	73	60	1:400	1:400

Immune A—Animals receiving the multiple subcutaneous injections in the back from 1-5 days after the immunizing intravenous injection.

Immune B—Animals receiving the multiple subcutaneous injections in the back from 6-12 days after the immunizing intravenous injection.

Hyperimmune—Animals which had received 4 intravenous injections at intervals of 5 days before the multiple subcutaneous injections in the back were given.

6-12 days. Allergic reactions are likely to take place in from 6-15 days after an initial injection. In the first division the concentration of antibodies was low never being above 1:200 at the time of multiple subcutaneous injections. In the second division the concentration was high 1:6400.

To determine whether a hypersensitiveness rather than the high antibody content in the serum was responsible for the greater frequency and larger nodules, 8 animals were highly immunized by giving 4 intravenous injections at intervals of 5 days. These animals were then given the multiple subcutaneous injections in the back. In the 8 animals there were 9 nodules out of a possibility of 160. In 9 per cent of the injections with the larger doses and 2 per cent of the injections with the smaller doses there were nodules. The microscopic structure of the nodules was similar to that seen in the normal and the other immune animals. The agglutinating titer was high 1:256,000 and 300,000. Since so few nodules developed in the 8 hyperimmunized animals it was evident that the increase in frequency and size of nodules in the second division of the immune animals was not due to the increased concentration of the antibodies but that it was most likely due to an allergic reaction as in animals made hypersensitive from an injection of streptococci in agar.

The hypersensitive animals were injected in one place subcutaneously with 5 cc of melted agar at 45° C. heavily seeded with streptococci. An abscess regularly developed at the point of inoculation. Multiple subcutaneous injections were made from 12-15 days later as in the normal and immune animals.

The gross reaction in this group of animals was pronounced. With the larger dose all but one of the

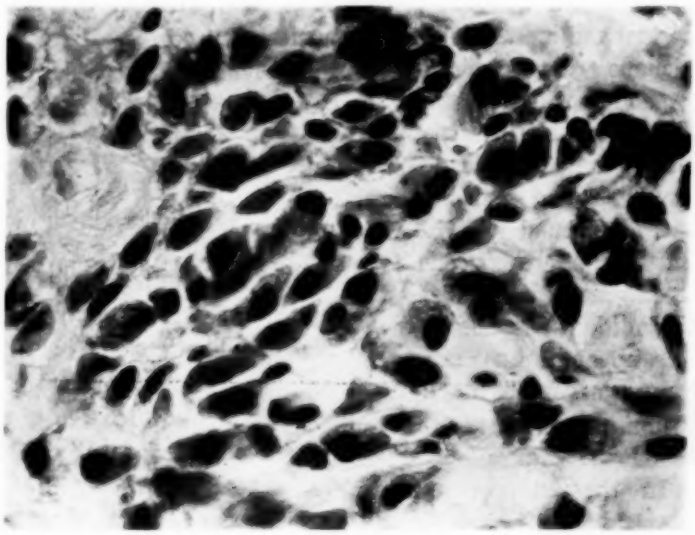

FIG. 1. Polyblastic nodule.

12 showed subcutaneous nodules and with the smaller dose nodules were present in all but 3. With both doses there were many nodules most of which were large and showed abscess formation. With the larger dose 73 per cent of the injections showed nodules and with the smaller dose 60 per cent (Table 1). It is obvious that the reaction in this group was definitely more extensive than in the other 2 groups.

The microscopic type of reaction showed a more pronounced exudation than in the normal and immune animals especially in the large nodules which were regularly abscesses. The smaller nodules showed the polyblastic type of reaction.

It was evident that the greater degree of reaction or hypersensitiveness so pronounced in this group was not due to a high antibody content since the agglutinating titer in none of the animals was ever above 1:400. The hypersensitiveness seemed to depend upon something which was not present in the normal and immune animals. The conspicuous thing which was present in group 3 and absent in groups 1 and 2 was the primary abscess resulting from the injection of the agar heavily seeded with streptococci. Something bound up with the abcess seemed to be responsible for the hypersensitiveness. What this substance or condition associated with the abscess is, apparently has not been determined by workers in immunity.

In conclusion it may be said that in the normal animals few lesions were produced. In the immune animals when the subcutaneous inoculations were made before the sixth day after the immunizing inoculation practically no lesions were present. Those animals in which the subcutaneous injections were made in from 6-12 days showed a greater frequency than did the normal animals. This greater reaction was probably due to allergy since other animals highly immunized from several intravenous injections did not have the increased reaction. On the other hand a retardation was evident. In the hypersensitive animals gross lesions, often large abscesses, were practically always present with both the larger and smaller doses.

Two types of cellular reaction were noted in all 3 groups: (1) the exudative, generally with necrosis and abscess formation, and (2) the polyblastic reaction. The cells chiefly found in the exudative reaction were polymorphonuclear leucocytes. In the polyblastic lesions there were regular and irregular mononuclear and multinucleated cells with basophilic cytoplasm, plasma cells, eosinophiles, lymphocytes, and often a few polymorphonuclear leucocytes. In some nodules the polyblasts appeared to have wandered in, while in others they appeared to have developed from the existing cells in the region of the nodules.

No difference could be detected in the character of the polyblastic reaction in the nodules in the normal, immune, or hypersensitive animals. Polyblastic inflammation free from abcesses was less common in the hypersensitive animals since the nodules were larger and the larger nodules regularly became abscesses.

It appears evident that the polyblastic type of reaction which is charac-

teristic of the lesions in human rheumatic cases does not depend primarily upon a hypersensitive state when produced experimentally in animals. This reaction may be produced with larger doses in both normal and immune animals. However, doses which in normal or immune animals have no noticeable effect or produce only small firm polyblastic nodules, will in hypersensitive animals stimulate the production of definite nodules many of which are extreme enough to be definite abscesses. The relationship between allergy and the polyblastic type of reaction, as seen in human rheumatic and experimental streptococcic lesions, appears to be not a qualitative but a quantitative one. This quantitative relationship may help to explain the pathogenesis of human rheumatic lesions in many cases.

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Embolectomy*†

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An attempted embolectomy was first reported in 1895, still this operation is quite rare in this country. Less than 20 cases were reported from the United States and Canada according to Pemberton in 1928. Reports are rare because the diagnosis is not made, or if made, it is not recognized as a surgical condition. It is the internist or general practitioner who sees these patients at the time when operation offers most, and an opportunity has been lost if he does not call the surgeon before gangrene has appeared. It is with the hope of keeping the subject before the profession until it becomes common knowledge to all that this accident is an urgent surgical condition that this paper is written.

In recent literature this subject has been so repeatedly reviewed that no attempt will be made here to give a complete review, but merely to stress some features of special interest to the internist and give a brief report of two cases, with one successful result. A complete review is to be found in the report of Einar Key (Acta Chir. Scand., 1921-22) or in that of Marco Petitpierre (Deutsche Zeit. für Chir., 1928).

The largest group of collected cases, i.e., 118, were reported by Petitpierre in 1928. Of the 95 cases collected by Key of Sweden up to 1925 only about one-half were included by Petitpierre because the others have not been published, being personal communications to Key. A great number of embolectomies performed have never been published, and no doubt they were for the most part unsuccessful cases, since one is more prone to report a successful case. Therefore when Petitpierre reports 34 or approximately 29 per cent of all cases successful in these 118, it is more favorable than if all cases were reported.

A thrombosis is practically always the source of an embolus. A calcified plaque becoming dislodged from the aorta is the only exception. This possibility is mentioned in the literature, but has not been the proven cause of any case. In 6,140 autopsies studied by Bull, there were 15 cases of extremity embolism. Thrombus formation was demonstrated in one or more of the cardiac cavities in 13 of these cases; the primary thrombosis was presumably in the aorta in the other two. Heart disease, he concludes, is the chief source of embolism; aneurism of

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the aorta and arteriosclerosis are only seldom the source. The primary thrombus may be dislodged *in toto* and its site at autopsy impossible to determine. The primary disease was mentioned in 104 of the 118 cases collected by Petitpierre. It was heart disease alone in 60 cases (approximately 58 per cent); arteriosclerosis in 4; syphilis in 2; it followed operation, delivery, or abortion in 23 cases and it followed infection in 11. The primary disease in the other cases was one each of widely different diseases. Mitral stenosis is the most common mitral disease causing embolism. It was present in 18 of Petitpierre's collected cases. Venous thrombosis and arterial emboli of the extremities were associated in only two of his cases and an anatomically open foramen ovale was found in only three of the cases collected by Petitpierre.

Embolism was demonstrated in other parts of the body as well as the extremity in all except one of the 15 cases found in autopsy material reviewed by Bull. These additional emboli were found in the lungs, nine times; kidneys, nine times; spleen, seven times; brain, four times; and in the intestine once. A complete search for evidence of other emboli should not be neglected where embolism is suspected in the extremity. This multiplicity of emboli was demonstrated in the case of an elderly, extremely obese woman with diabetes who developed an embolus in the popliteal artery while a patient at the University Hospital. A large vegetation on the aortic valve and an abscess at the base of the left lung was demonstrated at post mortem; this abscess was due to an infected embolus.

Emboli lodge at the bifurcation of an artery or the origin of a large branch, occluding both vessels as a rule. Vessel spasm, according to Petitpierre, is set up by the irritation of the embolus in the vessel, and this spasm plays a rôle in fixation of the embolus. Improvement sometimes seen in an extremity within the first 24 hours after lodgement of the embolus, he states, is probably due to relaxation of this spasm which lasts several hours, always less than 24 hours. Sufficient collateral circulation cannot develop in this short time to explain the improvement.

The frequency with which the various arteries are affected is well illustrated by Figure 1, taken from Petitpierre (Deutsche Ztschr. f. Chir.). This illustrates the location frequency in his 118 cases.

Gangrene follows more often if the circulation is occluded by an embolus than if it is occluded by ligature of the artery at the same point, because at the bifurcation of an artery or at the origin of a large branch emboli usually lodge, and both vessels are occluded, secondary thrombus formation results, extending rapidly in a distal direction and a clot also extends proximally to the origin of the next large branch. The collateral circulation is still further occluded by this thrombus. Beginning secondary thrombus formation was observed by Key as early as two hours after lodgement of an embolus. A secondary thrombus 86 centimeters long was present 12 hours after the lodgement of the embolus in a patient operated by Sandberg. Sec-

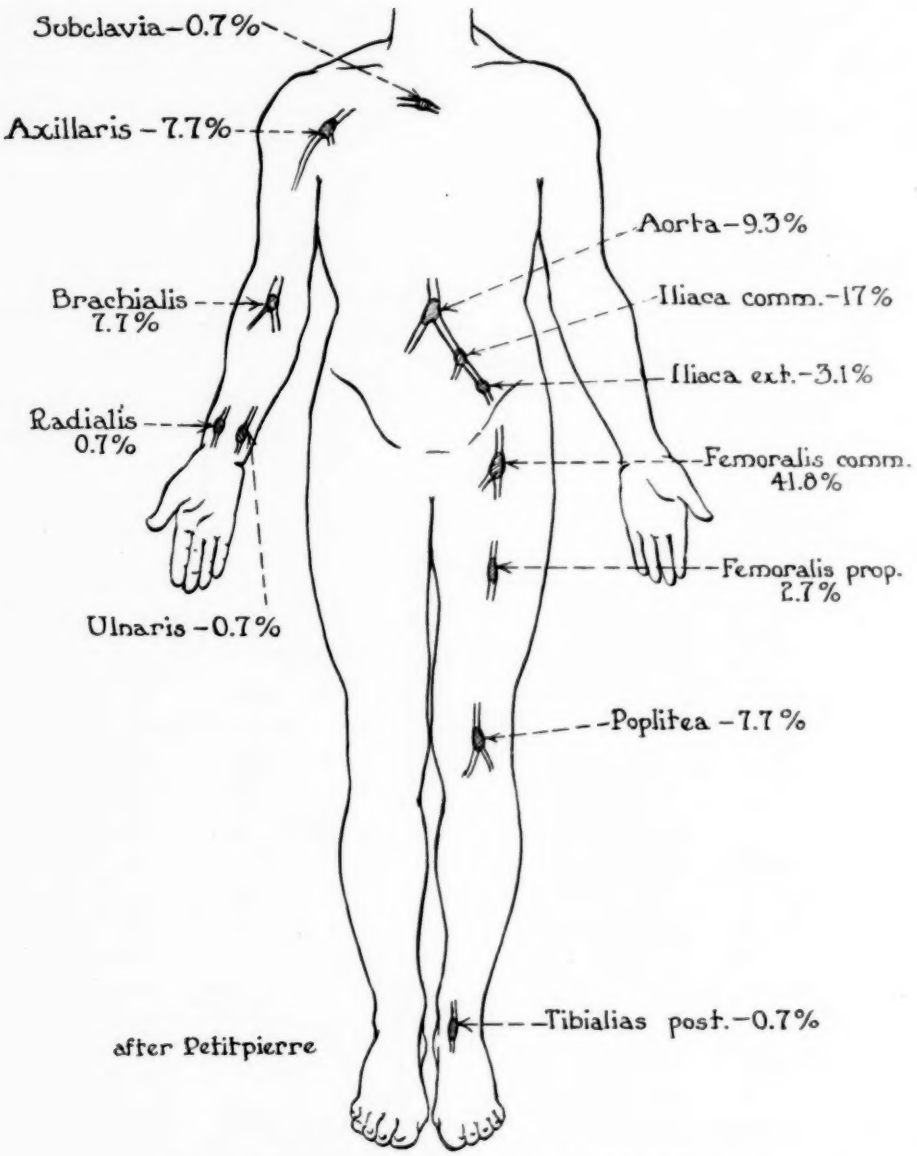

FIG. 1. Frequency of embolism in different arteries.

ondary thrombosis, however, may be slow to form. There was no thrombus in a patient operated by Ipsen two days after the occurrence of the embolus. The proximal secondary clot does not form until there is complete occlusion of the lumen of the vessel by either the embolus itself or the secondary thrombosis.

The prognosis depends upon many factors. Death in most cases is cardiac, i.e., the primary disease. The age of the patient and arteriosclerosis influence the prognosis in embolectomy. The intima in arteriosclerosis is easily injured and thrombosis occurs after operation. A patient 82 years of age, however, has been successfully operated. Massage to break up the clot and cause it to pass more distally is advised by Key, if there is high grade arteriosclerosis. According to Nyström, eight or ten cases have been published where massage was followed with good results.

Early operation is most important in embolism. Delay allows the embolus to become adherent. Removal is then more difficult and the intima more likely to be injured causing thrombosis after operation. Secondary thrombosis when extensive may be very difficult or impossible to remove.

The importance of an early operation is demonstrated in the following table of results compiled by Petitpierre.

Time between occurrence of embolus and operation	Circulation restored		Circulation not restored	
	Cases	Percent	Cases	Percent
1- 5 hours	24	58	19	42
6 10 "	15	68	7	32
11-15 "	6	46	7	54
16-20 "	2	29	5	71
21-24 "	1	14	6	86
Over 24 "	8	24	26	76

Similar results are reported by Key, who concludes that the prognosis should be good if operated in the first 10 hours but rapidly becomes worse thereafter.

In the upper extremity the prognosis is better than in the lower following occlusion of the vessels by an embolus. That gangrene is less frequent in the upper extremity following occlusion of the vessels by ligation has been demonstrated by Wolff and also by Heidrich. There are however other reasons why the prognosis is better in the upper extremity. Surgical approach is more difficult in the abdominal aorta, the iliac vessels and the popliteal vessels. A greater portion of the arterial bed is cut out of the circulation in an embolus of the lower extremity and this (first mentioned by Wildhopf) throws an extra load on the heart which is the site of the primary disease in most cases. A comparison according to location in 17 cases operated in the first ten hours after the occurrence of the embolus is given by Key. Eight were successful. His results are given in the following table:

Site of Embolus	Successful Cases
Axillary or brachial artery	3/4 of all cases
Femoral artery	1/2 of all cases
Iliac artery	1/3 of all cases
Aorta	1/7 of all cases

Multiple emboli, if present in an extremity, prevent complete restoration of the circulation after removal of the

most proximal one. Careful examination of the circulation should, therefore, be made immediately after operation, and if another embolus is present this should also be removed.

The symptoms of a typical case are pain, usually sudden and severe. There is a cold feeling in the extremity, a heaviness in the extremity and loss of sensation. Objectively there is a discoloration of the skin, cyanosis or an appearance described as marbleing of the skin. There is a lowering of the temperature in the distal portion of the extremity with a sharp line of demarcation between this and the warmer skin more proximal. There is a loss of reflexes and a variable amount of paralysis. Pulsations in the arteries are absent. The embolus may be palpable.

In the differential diagnosis, embolism is most likely to simulate thrombosis. The onset in embolism, however, is more sudden; there is heart failure and cardiac thrombosis or some other cause for an embolus as infectious disease or recent operation. Emboli in other parts of the body should be looked for because they are almost always multiple. In thrombosis a long history of such symptoms as the extremity going to sleep, neuralgia, rheumatic pains, and circulatory changes with cyanosis of the extremity are common. Hematomyelia and transverse myelitis may simulate embolism. There are no circulatory changes in these conditions, but there are neurological findings sufficient to differentiate them from embolism.

The treatment is immediate operative removal of the embolus and secondary thrombus if this is present. Massage is indicated only in certain selected cases.

Two embolectomies have been performed in this Clinic recently with one successful result. They are here briefly reported.

Case I. The patient was a young woman 22 years of age. She had heart trouble for 12 years according to her history. The present attack began with vomiting 18 days before admission to the Hospital. This vomiting continued for a period of two weeks. She noticed her heart was beating with unusual rapidity and that she was cyanotic the day after the onset of this vomiting. A physician was called and she was given digitalis. The pulse was 150 and irregular. The next day the pulse was 80 but irregular. Three days later she was given quinidine, and the following day the pulse was regular. There was less cyanosis and dyspnoea. She steadily improved from this time until the day of her admission to the Hospital. A sharp cramp-like pain occurred in her abdomen the day she was admitted. Immediately numbness, pallor, and pain occurred in the lower extremities. Approximately 30 minutes after their onset, the abdominal pain and the symptoms in the right leg disappeared but the pain in the left leg continued with such severity that morphine was administered. (The embolus at this time became dislodged from the bifurcation of the aorta and passed into the left iliac artery.)

Physical examination revealed a young woman very dyspneic and cyanotic, with no palpable radial pulse and a very irregular apical pulse varying between 110-130 pulsations per minute. A loud systolic murmur was heard at the apex transmitted through the axilla. All extremities were cold and cyanotic. The popliteal pulse was interpreted to be faintly palpable in both legs. The left leg was entirely anesthetic and paralyzed.

Arteriotomy was performed immediately after admission to the Hospital. An embolus and thrombus were found in the left iliac and femoral arteries. These were removed but circulation was not established in the extremity. A more distal incision

was made and more thrombus was removed. Still the circulation in the left leg was not re-established and the patient died a few hours later.

Case II. A man 58 years of age was admitted to the Hospital in January 1926, complaining of a swelling in the right scrotum which proved to be a hydrocele and a hernia. He also complained at that time of dyspnea which had been present for 20 years. This dyspnea made it impossible for him to sleep in a prone position. The cardiac condition was considered to be an aortic stenosis with aortic insufficiency and cardiac decompensation.

Because he had developed edema and ascites he returned in May, 1927. In June 1927, he was re-admitted with cardiac decompensation and ascites.

Again with edema and ascites he was admitted in May 1928, and it was demonstrated at this time that he had auricular fibrillation.

With the same complaint of edema and ascites he was re-admitted September 5, 1928. Six days after admission to the Hospital he developed an embolus for which embolectomy was performed. The attack began at 3 a. m. with severe pains in the left thigh and leg. A distinct pallor of the foot was evident and there was no pulsation in the vessels. Anesthesia of the distal portion of the leg was present with paralysis of all the muscles below the knee. The skin of the foot and leg was cold. Nine hours after the onset of his pain the patient was operated for embolus which was thought to be lodged in the femoral artery at the profunda femoris. At this site one embolus was found, after the artery was exposed but while it was being elevated the embolus became dislodged and then pulsations were present throughout the exposed portion of the femoral artery. Pulsation was also noted in the popliteal artery at this time although it had not been present before the operation. The embolus had become dislodged and passed down to the bifurcation of the popliteal artery into the anterior and posterior tibial arteries.

The patient was again taken to the operating room five hours later and the popliteal artery exposed. The embolus was in the terminal one and one-half inches of the popliteal artery. It was removed, and there was free flow of blood from arteriotomy wound when compression of the artery either above or below the incision was released. Immediately after operation the anesthesia and paralysis were found to have disappeared almost completely. Pulsation was present in both the popliteal, tibial, and dorsalis pedis arteries. An uneventful recovery followed and he was discharged from the Hospital 39 days after operation (October 20, 1928).

He returned December 11, 1928, with ascites and swelling of the left leg. There was good pulsation in the arteries of the left foot at this time. He was discharged January 12, 1929. For ascites he returned again March 18, 1929. There was no swelling of the left leg at this time. Ascitic fluid was again removed and he was discharged March 26, 1929. He died the next day at his home. This attack began about three hours before death with pain in the right leg and the left elbow. The family physician who attended him at this time considered embolism the cause of death.

SUMMARY

1. Embolectomy of the arteries of the extremities is not recognized as an urgent surgical condition by many internists and general practitioners.

2. The primary disease in most cases is cardiac, and of the various cardiac diseases mitral stenosis is the most common cause of embolism.

3. Embolectomy should be performed as soon as the diagnosis of embolism is made and certainly before gangrene has appeared.

4. A single embolus is rare. When suspected, search should be made for evidence of emboli in lungs, kidneys, and spleen.

5. Emboli lodge at the bifurcation of large vessels or the origin of a large branch.

6. Secondary thrombosis follows the lodgement of an embolus. This obstructs the collateral circulation.

7. For re-establishment of the circulation the prognosis becomes rapidly worse if the patient is not operated within approximately ten hours after the embolus has occurred.

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Preliminary Results of Resection of Sympathetic Ganglia and Trunks in Seventeen Cases of Chronic "Infectious" Arthritis*

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RESECTION of lumbar sympathetic ganglia and trunks for the relief of so called chronic infectious arthritis (rheumatoid arthritis, arthritis deformans) of the lower extremities was first employed in June, 1926. The operation was performed by Adson at the request of Rowntree. The rationale for the procedure, and the immediate results of the operation on the first patient, and the subsequent course of the disease have been presented by Rowntree and Adson. The degree of relief experienced in the lower extremities, particularly in the feet, caused the first patient to request earnestly a somewhat similar procedure to relieve the pain and disability in the upper extremities. Hence, in November, 1928, resection of the cervicothoracic sympathetic ganglia and trunks was done in an attempt to relieve the pain and disability of the arthritis of the upper extremities. These results likewise were recorded and in another article, the results in the first six cases of our series were described. The relief of disability of the joints, during the first months after operation was sufficiently satisfactory so that it was decided to determine further the limitations and value of resection of sympathetic ganglia and trunks in arthritis of the type generally believed to be of the chronic, nonspecific, infectious form.

To date, eighteen bilateral operations of the type mentioned have been performed on seventeen patients.

One patient underwent both cervical and lumbar procedures. Of these, fifteen operations concerned the lumbar, and three the cervicothoracic sympathetic apparatus. Although this represents a fairly considerable experience, the number of cases is too small and the time elapsed too short to permit of other than tentative opinions regarding the selection of patients for the procedure, its indications, its contra-indications and its results.

Although this report will include a summary of the results in all cases to date (seventeen cases; eighteen operations) the data regarding the last elev-

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en will be given only by way of a general statement, for in them, less than six months has elapsed from the time of operation. The report also will deal with the further progress, since our last report, of the first six patients who were subjected to the operation. These have been emphasized because the time which has elapsed since operation in each instance is sufficiently long (six months to three and a half years) to permit of some idea as to the nature and permanency of the changes induced, and the correctness of our criteria for the selection af cases. They include, furthermore, patients who illustrate what are probably different phases of chronic infectious arthritis (periarticular, chrondro-osseous phases).

Report of Cases

Case 1.—A woman, aged thirty-four years, with crippling, generalized polyarthritis of six years' duration, was subjected to resection of the lumbar sympathetic ganglia and trunks in June, 1926, and to resection of the cervicothoracic sympathetic ganglia and trunks in November, 1928. Her progress has been definite. Since dismissal she has suffered somewhat from tenderness and pain between the shoulder blades in the region of the surgical scar.

In the autumn of 1928 she wrote that she had not had any further pain in the lower extremities, and that she still felt occasional twinges of pain in the left wrist on washing dishes and in the right shoulder on carrying heavy weights. About this time also, she informed us that she was conferring with the president of the railroad concerned in an accident which she had sustained and requested from us a letter concerning the nature of her illness and its relation to the railroad accident. During this period, when a pension was pending, she wrote that she had suffered a relapse of the arthritis.*

*Nervous stress and strain probably play a part in the pathogenesis of this form of chronic arthritis. A second patient has not done as well as we expected; a question of disability insurance is concerned. A third patient suffered a relapse during the serious illness of her mother.

Following the receipt of a letter announcing that she had been awarded her pension, she wrote that she had improved greatly. The relief of the condition in her lower extremities may therefore be considered complete and that in the upper extremities may be graded as very considerable. In this case, the arthritis was very largely periarticular.

Case 2.—A girl, of Greek parentage, aged sixteen years, with polyarthritis of the lower extremities of two years' duration underwent resection of the lumbar sympathetic ganglia and trunks and returned after two months; at that time she was able to walk a distance of 100 to 200 feet without assistance. Improvement continued so that at the end of five months after operation she could walk comfortably a distance of four city squares and had taken up dancing again. Pain had almost disappeared from all the joints of the lower extremities. This also represents a case of the periarticular form of arthritis. Development of arthritis elsewhere in the body has not been reported.

Case 3.—In a woman, aged forty-four years, the condition ran a definitely febrile course, with extreme anemia, marked swelling of the joints, striking muscular atrophy, and no improvement of the condition of the joints after seven and a half months of treatment in hospital. Following the cervicothoracic operation in May, 1929, and prior to her dismissal on the forty-fourth day, the condition of the upper extremities was markedly improved, the swelling decreased at least 50 per cent, and the function of the hands and arms was restored at least 50 per cent. Her condition continued to improve considerably for a number of weeks. At the end of four months she wrote that the condition of her hands was becoming stationary. At the expiration of seven months she reported that her general condition was decidedly improved, but that that of her legs was unchanged

and that she still was bedridden. Later, she stated that she had had an exacerbation of the attacks and that her left hand was somewhat worse. However, she also stated in the same letter that she wanted to return for the lumbar operation for relief of the arthritis in her legs.

Case 4.—A man, aged twenty-six has experienced no relief of his main complaint, pain in the right hip. The arthritis was of long duration, twelve years, had resisted all forms of medical treatment, was destructive, and there were marked bony changes. Since his operation he has reported the continued presence of large, swollen lymph nodes below Poupart's ligament on the right side, and marked pain in the hip and lymph nodes on every attempt to move the right leg. To date, at least, the result here must be regarded as a complete failure so far as his chief disability is concerned.

Case 5.—A woman, aged twenty-one years, has shown definite improvement despite the diagnosis of bony ankylosis in the knees and hips. She returned home after a period of four to five months in the hospital. She then was able to walk alone and unassisted, although she had been completely bedridden for two years prior to operation. She has written that she still has considerable pain in her knees, and especially in her right hip, but that, once she is placed on her feet, she can walk around the house comfortably. She has suffered one mild exacerbation of arthritis. Although there is still marked limitation of motion, she has acquired an unexpected degree of motion in the knee, and, to a less extent, in the hips. The results to date have been satisfactory, especially in view of the bony changes and the marked degree of ankylosis.

Case 6.—A woman, aged thirty-four years, with generalized arthritis, returned home eight weeks after resection of lumbar sympathetic ganglia and trunks. Her condition was markedly improved so far as all the joints of the lower extremities were concerned and she could walk up and down stairs, a feat that had been impossible to her for the preceding eight years. Her physician, who visited the clinic two months after her return, reported continued marked improvement and stated that she went about everywhere with little, if any, trouble in the feet and legs. However, she replied personally, at the end of six weeks, saying that she had had an exacerbation of arthritis at the time that a sinus in the wound had discharged a stitch. There was some involvement of the legs, but this was not comparable to the exacerbation in the arms. The arthritis is progressing in the upper extremities, but its progress has slowed up remarkably in the legs.

Comment.—The results after six months are unusually satisfactory in at least three of the six cases. The degree of improvement was greatest in cases of the periarticular type. The acceptance of the other three patients for operation was in the nature of clinical experimentation. Their cases were advanced, had not responded to other treatment, and in the light of our present experience would not now be accepted for operation.

The results in the remaining eleven cases can more appropriately be covered by a simple statement. Marked relief from pain was encountered in many of the cases of the periarticular type but relief was less marked and slower in onset in cases with osseous changes.

If all seventeen cases are considered, in six, chrondro-osseous changes were definite or advanced, as indicated by roentgenologic evidence. In not a single instance was recovery complete in this group. In our opinion, the relief from pain, however, justified the procedure in most instances. Considerable improvement was noted in five. Of the eleven cases of the periarticular type, marked improvement

was seen in nine. In fact, six of these have had but little pain in the extremities since operation, and in all except two the improvement has been marked.

Postoperative Complications

Complications following operation have not been serious except in one case. Ileus developed in two instances following the lumbar operation, and in one case was rather extreme. Rather profuse diarrhea was marked in three other cases, but in no instance was it serious. In one case, following resection of cervicothoracic sympathetic ganglia and trunks rather mild pleurisy developed, and in another case, mild pleurisy developed on the twelfth day following the lumbar operation. Following the lumbar operation on two patients a rather acute exacerbation developed in the metacarpophalangeal joint of the right thumb. Pains in character resembling that of erythromelalgia were observed in two cases over a period of approximately a week, but these were readily controlled by elevation of the part concerned. Our first patient has suffered considerably from pain below the shoulders, about the operative scar. Personnel neuritis was unmasked by the operation in one case. On resumption of activity, myalgia has been noted in most of the cases. It is, however, not severe and is of short duration. Deaths have not occurred in the series either immediately after operation or in subsequent months or years.

Selection of Patients for Operation

Selection of our first patient was founded chiefly on the presence of neurocirculatory changes in the extremities and long-standing chronic arthritis which apparently was unresponsive to the usual methods of treatment. There were no gross bony alterations in the joints. The hands and feet were cold and clammy as well as swollen and painful. Because of the warming up of the extremities after resection of sympathetic ganglia and trunks in Raynaud's disease, it seemed reasonable to expect a similar result in the cold extremities of patients with arthritis, and it was hoped that with the additional warmth, pain would cease. The selection of the first patient seems justified.

In selecting patients with chronic infectious arthritis for resection of cervical sympathetic ganglia and trunks, six requisites have been adopted up to the present time.

1. The arthritis should be chiefly pariarticular in type, with little, if any, bony alterations (destruction or hypertrophy) except atrophy, and with little, if any, deformity except that resulting from periarticular changes.

2. The patients should present neurocirculatory changes evidenced objectively by cold, clammy, sweating hands or feet, and subjectively, by a feeling of coldness, numbness and tingling.

3. The circulatory deficiencies must be capable of correction, indeed of overcorrection, under the influence of release from control of the sympathetic apparatus. The possibility of such correction can be demonstrated by the "vasomotor index" (Brown); a definite increase of the cutaneous temperature of the extremities perhaps three to five times greater than the in-

crease of the temperature of the mouth after typhoid vaccine (50,000,000 bacteria) has been given intravenously.

4. The patient should be, preferably, aged less than thirty-five years, and not more than forty or forty-five years.

5. The arthritis should have been progressive and the main disability should be confined to the extremities, particularly to the hands and feet.

6. A reasonable period, probably a minimum of six months, of intensive, systematic treatment by the more established, less radical procedures should have been allowed.

Exceptions in selection of patients.—In the majority of our seventeen patients, all six of the requisites were met. In six cases, exceptions were made in that patients were accepted for operation, although the joints of the extremities involved presented fairly marked bony changes. In these cases, the exceptions were made deliberately because of lack of improvement in the condition after a prolonged period of intensive treatment, because of the painful, progressive character of the arthritis, and in order to test out the limits and values of the operation.

In one case, because of the rapid progression of the arthritic disability, the economic circumstances necessitating an early return to work, and failure of previous treatment to give appreciable benefit, operation was advised rather soon after the onset of the arthritis.

How far the eventual results will justify these exceptions cannot be stated. In some cases, the results to date seem to justify their selection, whereas in other cases failure materially to alter the disability must be recorded. This indicates that until more is known regarding the use and limitations of resection of sympathetic ganglia and trunks for cases of chronic infectious arthritis, acceptance of patients who do not present the six criteria mentioned should be made with caution in order not to discredit unjustifiably the value of the operation for that type in which it seems to be particularly suitable.

It will be seen that the ideal subject for this procedure is one who is young, who has the periarticular (rheumatoid, atrophic) variety of chronic infectious arthritis, and that chiefly in the hands or feet. To a less degree the subject in which the elbows and knees are affected is suitable. In our comment we shall deal with the indications for resection of sympathetic ganglia and trunks for infectious arthritis of the spinal column, hips, and shoulders, and to its extension into the field of chronic traumatic, chronic gouty, and chronic senescent arthritis.

Postoperative Treatment

The postoperative treatment is of considerable importance. Because of the diminution or absence of pain in the joints, there exists the temptation to attempt a program of overactivity. In the results of the treatment it will be seen that in certain instances pain is more favorably and more rapidly affected than some of the other phenomena of the arthritis, such as swelling and stiffness. Pain is but one signal, and when it is removed, care must be taken not to overexercise the joints until subsidence of the other phe-

nomena indicates the appropriateness of increased activity. Excessive weight-bearing should be avoided, especially in obese persons. Physiotherapy, active and passive motion, and massage are desirable subsequent to operation, since they complement the increased heat in the affected members, which is the result of the operation. When necessary, mild analgesics may be supplied.

In general, a program of conservatism is desirable, and the amount of activity should be guided by the condition of the patient; the pain on exertion serves somewhat as an index. Certain orthopedic measures may be indicated as supplementary measures, such as manipulation of joints and extension. In cases of arthritis of the knees, with previous flexion deformities, braces may be necessary until improvement takes place. When the patient has been bedridden or confined to a wheel chair for a considerable period of time, walking should be undertaken, at first with the aid of a walker, and later with crutches or a cane, until the patient's equilibrium and confidence are restored. The application of correct shoes is important. It will be recalled that painful, flat feet, associated with disability elsewhere, are complained of by a group of patients who consult orthopedists.

In general, foci of infection will have been entirely removed before the patient presents himself as a possible subject for resection of sympathetic ganglia and trunks. If they have not, care should be taken that all foci of infection are removed before dismissal of the patient. Full instructions in physiotherapy to be applied at home are given to the patients and their own efforts should be supplemented by an adequate program of physiotherapy to be given under professional supervision.

COMMENT

The nature of the circulatory alterations in arthritis.—Unfortunately, the nature of the circulatory changes in arthritis is not definitely known. Hence, it would be unwise to make assumptions concerning them. We have spoken of them in an earlier communication as vasospastic phenomena, without, however, attempting to explain their nature.

We can make our position clear, perhaps, by first acknowledging that we do not know with certainty that this form of arthritis is infectious, and that we do not understand the nature of the derangement of the circulation or the part that the nervous system plays in these changes. The known facts are as follows: Prior to operation, the hands and feet are cold and clammy and bathed in sweat. Studies of transference of heat from these extremities, in the Stewart-Keggereis calorimeter, indicate a low normal value. Mottling and cyanosis of the skin of the hands and feet are common. The study of the capillaries of the nailfolds reveals capillaries larger rather than smaller than normal, and with a very slowly moving blood stream. Trophic changes, particularly of the finger nails and toe nails, are very common, as is atrophy of the muscles. The feet are often painful at rest, particularly on compression and on motion.

After resection of sympathetic ganglia and trunks, the following changes are noted: The hands and feet become warm, pink and dry. The temperature increases anywhere from 5 to 10°C. Sweating ceases. Pain decreases immediately and in some instances disappears almost completely; disappearance is earliest in the periphery of the extremities, and later, to a lesser degree, in the more proximal joints.

Transference of heat, as measured in the calorimeter, increases anywhere from 100 to 500 per cent. Under the microscope the capillaries now appear narrower, and the flow of blood is markedly increased. Trophic changes tend to disappear. Swelling about the joints tends to subside and the muscles tend to return to normal size and function. The nails become normal in consistence and appearance.

From what has been said, it is not likely that the arthritic changes are brought about by spasm of the large arteries. Professor Krogh, with whom the problem was discussed, felt that the most likely explanation was that there is an arteriolar constriction, with peripheral dilatation of the capillaries. This constriction ceases after resection of sympathetic ganglia and trunks and permits a more rapid and normal flow of blood, with increased tonus in the walls of the capillaries. For the time being, at least, we will refer to these changes simply as "neurocirculatory" without any attempt to explain them.

The use of resection of sympathetic ganglia and trunks in the general field of arthritis.—Resection of sympathetic ganglia and trunks is not indicated in all forms of polyarthritis. Hench has classified arthritis, on the basis of presumptive evidence, as follows: (1) infectious, (2) traumatic, (3) senescent, and (4) chemical, for example, gouty. This classification is particularly valuable for within itself it suggests a rational basis for treatment.

The group of cases of chronic arthritis with which we have dealt may belong to the infectious type, although this is not yet proved. Acute involvement of the joint precedes these chronic manifestations in certain instances, but by no means in all. These neurocirculatory manifestations are secondary to what appears to be infection, in some instances, but in other cases they seem to be primary in origin. Whether primary or secondary, they may respond to resection of sympathetic ganglia and trunks and when present they constitute an indication for the procedure.

It is possible that in other forms of arthritis, resection of sympathetic ganglia and trunks may be of value. This is a matter that can be settled only by time and clinical experimentation. The rational indications for its use in these other forms of arthritis are not yet determined. Until more is known, we wish to advocate the employment of resection of sympathetic ganglia and trunks only in the periarticular form of arthritis that has been described and especially in cases in which the chief disability is in the peripheral parts of the extremities, and generally in cases in which there are neurocirculatory phenomena. Otherwise, it may be employed in a haphazard and irrational way and quickly may come into disrepute. In certain instances of infectious periarticu-

lar arthritis in the extremities, the appearance of neurocirculatory phenomena may be rather long delayed after the onset of the disease. In some of these cases, the rapidity of progression. degree of disability and pain, and lack of response to other treatment may justify the operation in spite of the absence of definite neurocirculatory alterations.

Summary and Conclusions

1. These seventeen cases serve to indicate the value and limitations of resection of sympathetic ganglia and trunks in the treatment of chronic infectious arthritis.

2. They demonstrate that the procedure is applicable both to the upper and to the lower extremities, and that the best results are obtained in the periarticular type of arthritis, associated with neurocirculatory alterations. In such cases, the relief from these vasomotor alterations, such as coldness, and sweating, is extremely gratifying. Indeed, if the operation is performed in an anatomically correct manner, sweating should be completely absent subsequent to operation.

3. The cases demonstrate that definite restorative influences are supplied to combat the trophic changes and atrophy of muscles such that in some cases function is restored to a considerable degree.

4. Our experience indicates that the effect of resection of sympathetic ganglia and trunks lasts for a period of at least six months and has lasted more than three and a half years. It promises to be of permanent value. The best results are obtained in the hands and feet; the results in the knees and elbows are less marked and slower in developing. The effect of the procedure in the hips and shoulders seems considerably retarded. The operation for arthritis of the hips and shoulders alone seems as yet not justifiable.

5. The presence of bony changes, revealed by roentgen ray, particularly in the knees and hips, suggests a less hopeful, indeed in some instances a hopeless, outlook. However, even when ankylosis is completely or partially established, pain while the subject is at rest may disappear, and pain on active motion may be alleviated wholly or in part.

6. Failure of the operation has been most apparent in joints, particularly in painful hips which still were movable but in which there were marked osseous changes.

7. For the present at least, we advocate this procedure for the one type that has been herein described, mainly periarticular arthritis with evidences of neurocirculatory phenomena, and which react to administration of typhoid vaccine with a high vascular index. The result in some of these cases, as far as the hands and feet are concerned, seem gratifying.

Remarks on Chronic Infections*

By Allen K. Krause, *The Desert Sanatorium, Tucson, Arizona*

THE time-limits set for the presentation of this address have led the author to restrict his attention to a particular type or group of chronic infectious processes rather than to attempt a synoptic discussion of certain broad features, mainly etiological, of chronic infections in general, the purpose that inspired the original title of his paper.

This particular group of chronic infections involves the lungs. It represents processes that are essentially focal, that is, localized. Its etiology is dubious, save that this is certainly non-tuberculous and its pathology, for months, years and even decades, may be no less dubious. Its consequences, there is reason to suppose, may be grave: indeed,—to anticipate a bit,—we are wondering whether often we may not here be dealing with the precursors or originators of conditions which, as finished or incidental processes, later present themselves to us as bronchiectasis, or bronchopneumonia,—recurrent or periodic bronchopneumonia,—or asthma, or even abscess. This group of pulmonary infections will never come to autopsic observation except through some accidental unrelated cause, when, if it did, it is questionable whether routine examination would detect a definite pathological condition. At its slightest or mildest it is doubtful whether examples of the group will overly impress the medical attendant, unless he has become alive and alert to their existence. At its worst he is likely to decide that he is dealing with bronchiectasis or chronic "pneumonia."

The clinical histories of patients with the type of pulmonary infection in question may vary much in details, but their general tenor is not uncharacteristic. Indeed, it is close attention to clinical history that above all else is likely to put the physician on the track of their recognition. Out of a rather checkered clinical past there usually emerges the prominent item that the subject—usually child or young adult—has been oversusceptible to colds, perhaps for years, and characteristically increasingly so as regards both number and severity. Then, in not a few, the recurrent winter cold takes a turn that is manifestly of more moment than a cold and is (rightly so) considered as bronchopneumonia. Following this appear persistent changes in the lungs, most often in base or midlung, when now these more permanent residua are conceived of as having originated in the recent pneumonia

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and as being the latter's unresolved remains. The point is that old focal changes had in reality antedated the pneumonia and that the latter has been merely an acute incident in the more or less prolonged course of a chronic process.

We may attempt a type-history, emphasizing that this will have many variants. Very often, if not most frequently, the patient is a child, six, eight, or a dozen years old, yet with years of medical concern, especially as to nose and throat, behind him. He was a healthy baby until a first acute illness like whooping cough or measles. After this he gradually, even insidiously, slipped into the category of "delicate child." Successive winters were sure to find him easy, and easier and easier prey to catching cold, until the approach of the cold season was anticipated with dread. In time, winter came to mean one long stretch of "bronchitis," so called, punctuated with acute febrile periods that put the child to bed. With the coming of warm weather, the bronchitis improves and fresh colds become fewer, until by midsummer the child is symtomatically sound; and he keeps symptom-free until the first pronounced autumn weather ushers into the inevitable new "cold."

The ordinary child of this type comes out of the winter a good deal run down, with blood, weight and vigor under par, and during the summer again builds up, often to normal capacity. The very fact that such a child in time comes to be over-protected and coddled, in efforts to ward off the taking of cold, tends to soften him and increase his susceptibility to fresh attacks.

Meanwhile this child has usually made the rounds of the nose and throat clinics, and, usually too, has at one time or another had tonsillitis, adenoids, otitis media or sinusitis. Often one or several of these conditions has been chronic and recurrent. Often again all treatment has been directed to these appendages of the respiratory tract, with the idea that they alone have been responsible for the symptoms that rise manifestly from some disturbance lower down. One by one these upper respiratory conditions are corrected or removed, and often with a fair measure of success as the recurrent "colds" lessen or abate. But only too often by the time the throat, nose and ears are attended to, the over-susceptibility to colds seems to have become fixed, and these go on with even increasing frequency and severity.

It is now that an over-severe "cold" gets out of bounds and takes on the ear-marks of a bronchopneumonia. Now are found, perhaps for the first time, localized pulmonary changes, which remain after recovery from the acute illness. And now also the patient resumes his former condition of delicate constitution, and chronic bronchitic symptoms, but with the difference that he is now known to have a patch of râles or increased X-ray density out from the hilum or toward the base, where none was known to exist before, and this is presumed to be a spot left by his pneumonia.

Or it may be that, without suffering a pneumonic attack, symptoms of asthmatic nature make their appearance; and that these lead to unusual scrutiny of the chest; and that now a

midlung or basal pathological process is disclosed.

There is increasing evidence that in many of these children with oversusceptibility to colds, pulmonary changes, located more below midlung, have existed for a long time, and that they are the site whence originates the trouble that has afflicted the child for years. Under present conditions of practice it is likely that in the very great majority of cases they go unrecognized until the incidental occurrence of some more serious and better defined malady, such as bronchopneumonia or asthma, which sends the physician to a more thorough and assiduous examination of the chest. We believe that, if ordinarily practiced earlier, closer attention to the chest would bring to light many more focal processes of this type in patients who have not gone as far as the more severe manifestations. But we are also beginning to wonder whether many of these patients may not for a long time have small more or less permanent foci of non-tuberculous infection whose anatomical presence defies detection even by X-ray.

In other words, is there such a condition as permanent pulmonary change set up by infection of a chronic and clinically persistent or recurrent nature that is not demonstrable by ordinary diagnostic methods? If so, how frequent is it and how often can or does it assume more significant proportions? The reason for asking such questions is that it is only by supposing the actual occurrence of such focal changes as probable and not uncommon that we can come to an understanding of a series of clinical events that is by no means rare.

There is, for instance, the patient of varied age, as often as not a vigorous young adult, who comes down with a hard cold, marked by the usual symptoms and three or four days of moderate fever. The disease runs its usual course and convalescence is normal in every respect except that we are disturbed by the persistence of a few râles in a small localized patch at the base. On the strength of this finding we keep an otherwise recovered patient in bed, hoping that the râles will disappear. But they do not disappear promptly. They do not disappear with weeks in bed, as meanwhile a restive patient clamors to be let up and about his daily life. Time and again they will not fade out entirely until the coming of summer with its established warm season. Then, and not until then, does the chest become clear.

There is nothing particularly remarkable about this relatively common incident, nor would it be difficult to understand if this were all there always was to it. But some of these cases become puzzling when we find them in the throes of a fresh winter cold, say, the next winter. We observe the same symptoms, the ordinary ones of a hard cold. We hear râles. But—and this is remarkable—the râles are in the identical spot where we detected them the year before and whence they slowly disappeared. Further, the patient stages the same performance of a year previously; that is, carries the râles until summer with its sun and warmth rids him of them.

Some of these patients also gradually slip into a condition of permanent pulmonic signs, summer as well as winter, and of increasing disablement by recurrent winter colds. Arrived at this point, their general course is not materially different from that of the younger patient sketched above.

It is obvious that established bronchiectasis must have an antecedent development, and we ask ourselves whether these minor changes may form the nidus or the earlier phases of such a later more serious process. We also speculate as to the pathological (anatomical) nature of these essentially slight changes. They cannot be regarded as an ordinary chronic bronchitis, a diffuse involvement of the air-passages, for the lesions in question are essentially focal, thus resembling the beginnings of tuberculosis. But in such foci what tissues are involved and how are the component structures of the lung modified? Moreover, does there exist a permanent focal infection of the lung with microorganisms nesting continuously, to flare and erupt clinically from time to time?—or do the recurrent winter attacks of "cold" mean that with repeated fresh infections from without the newly received germs are accustomed to focalize in the same spot,—perhaps because this is a damaged and therefore a weakened patch of tissue?

It is difficult to entertain the last supposition. Limited time will not permit of an analysis of probabilities; but it is much more in line with newer concepts of infection in general to presume that a permanent and fixed and at the time perhaps latent focus of infection reactivates and takes on new clinical significance under the influence of the obscure biological and immunological agents which we know are set in motion by even the common cold. Our concepts of chronic infections have been changing radically of recent years, and among these newer ideas none is of more significance than the growing opinion, continually being fortified by new evidence, that clinical recurrences of varied features of infectious processes represent, not fresh infections, but renewed phases of clinical activity of infections long present but at intervals concealed. The case was long ago settled for syphilis, and is now universally accepted. That for tuberculosis had a rockier road, but the weight of evidence and general opinion is now overwhelmingly for it. That for gonorrhoea, essentially and significantly one of our most superficial infections, is well established, as too is the quite comparable case for diphtheria. Evidence accumulates that recurrent rheumatic fever and acute endocarditis represent acute phases,—episodes,—incidents in the life-history of a chronic, apparently deep-seated infectious process. And a growing acquaintance with the clinical histories and manifestations of these patients characterized, among other features, by an over-susceptibility to catching cold, engenders the conviction that many of them are in reality harboring relatively permanent, usually basal, chronic infectious processes.

If there are relatively permanent small foci of non-tuberculous infection in these patients, what are we to think regarding their pathological (anatomical) character? Sooner or later some of them come to observation, es-

pecially X-ray, as irregular patches of increased density, when, with or without râles on physical examination, they may be supposed to be mainly sclerotic formations in which have been involved the several elements of pulmonic structure,—bronchi, bronchioles, alveoli, etc. We have in mind now one particular case,—that of a child, five years old, who in June showed just this structural change after four years of recurrent winter colds, and who in August, following exposure, developed bronchopneumonia, confined to the patch in question. This now suddenly extended its boundaries. The impression conveyed was as though an old and relatively quiescent non-tuberculous infection had "slopped over", as it were, into pneumonia. Recovery from the latter was marked roentgenologically by a gradual drawing in of the area affected by the pneumonia as well as by a more rapid and complete disappearance of râles.

But what are the earliest changes,—earliest though on occasion lasting perhaps for years,—in such a focus which merely gives out a few persistent râles following a heavy cold, and this recurrently for several years with intervals of essentially normal breath-sounds between? Clinically there has never been a symptomatology to allow a diagnosis of bronchopneumonia. Perhaps, though, this is merely a question of extent of involvement, and it may be that essentially pneumonia had existed,—a pneumonitis or alveolitis, let us say, covering a very limited territory indeed. And, when signs persist in this region after prompt symptomatic recovery from the acute hard cold, it is not too much to suppose that, if not alveoli, then small air-passages—bronchioles as well as bronchi—have undergone changes that persist. Complete resolution has not terminated the acute inflammation; something more than mucosa had been involved; and rather lasting focal changes in the walls of the air-passages have resulted. We may speculate as to fibrosis with a concurrent limited lymphangitis of these structures. And, if this is the condition, how can a few alveoli escape participation in the process?

Let this go on for some years, and let it moreover be exacerbated and added to by ever-recurring "colds," and we arrive at an appreciation of how the field is prepared for the origin and development of localized bronchiectasis; or how are established foci that under proper excitants can set up bronchopneumonia; or how, more rarely, focal abscesses may arise; or how may be prepared the mechanism for "asthmatoid" phenomena.

For it is only a step from permanently damaged bronchioles to weakened bronchiolar walls, with focal bronchiectasis in the offing, as happens in focal pulmonary tuberculosis. (We are now thinking in anatomical terms only.) Or, if nests of microörganisms dwell on within these foci, occasional flarings into bronchopneumonia would seem inevitable; whence, in a minimal proportion of cases, further development to at least miliary abscess would be just as inevitable.

Clinically, we have been particularly interested in the asthmatic side of some of these cases. It is characteristic that symptoms of asthma do not appear at the beginning, but only after there has been a fairly long history of

the recurrent "colds," with presumably the chance for chronic pulmonary changes to develop. Now come the sudden attacks of coughing or wheezing, precipitated often by abrupt exposure to cold air or even by stepping with bare feet on a cold floor. As for the "asthma" there may be anything from transient wheezing to prolonged and severe attacks that superficially resemble classical bronchial asthma.

But we have thus far been unable to bring ourselves to identify what here seems like asthma with the classical disease. Features of hypersensitiveness have been conspicuous by their absence, as have too those of heredity. We are much more impressed by the probabilities of the mechanical side of the case. We remember the rich endowment of nerves and ganglia that Miller has pictured existing in the human lung, and recall particularly those findings of Miller's in which, in connection with focal pulmonary disease, nerves and ganglia were observed to be involved,—"enmeshed" as it were,—in the inflammatory or infiltrative process. Sometimes it was the nerves of supply to bronchial mucous glands, a finding that suggested an effect on bronchial secretions. We have seen long periods of symptomatic quiescence in these cases interrupted by sharp asthmatic attacks during which these foci, free from signs for a long time previously, gave out a wealth of signs, as meanwhile the temperature rose and the rest of the lung was relatively quiet. We wonder therefore whether a focus, placed right as regards nerves and ganglia, may not precipitate asthmatic symptoms through merely mechanical irritation.

Relatively early and minor focal infectious processes, such as we have been discussing, must be of every degree of duration, extent and significance. Many, perhaps most, no doubt disappear completely without ever having caused illness of any moment. But, as representing foci that may go on to some of the most serious of pulmonary diseases, they are to be regarded seriously. Many will no doubt question the dictum that they should be viewed at least as seriously as the minimal or early focus of tuberculosis that has thrown out warnings of activity. Yet when one sees the patient who gradually progresses to recurrent pneumonia or bronchiectasis one inclines to so radical a position. As in tuberculosis the time to get the condition therapeutically is at the beginning, a prime reason why the condition should be recognized in its incipiency. Even though not the trace of an anatomical change can be demonstrated, we must suppose that where there are long-continued basal râles, or râles at the same spot with recurrent colds, there must be a pathological focus,—a focus that represents a relatively permanent infection, harboring living microörganisms that await only the favoring agents to be aroused to renewed activity.

Even after the process is fairly extensive anatomically, it may be râle-free over long periods. But this need not mean that it has lost all capacity for mischief. With a fresh "cold" it again sends out sounds in abundance and gives out all the signs of acute reinflammation. These foci are prob-

ably never of no further moment until they have been completely healed and fibrosed.

It is particularly important to attempt the healing of these processes in children. Fresh exacerbations and progressions to the point of bronchiectasis can forecast as sinister a prospect as active tuberculosis. Nor should one postpone serious treatment until the appearance of one of the graver consequences of these foci.

Their treatment is tedious, and under ordinary conditions unsatisfactory in any environment that promotes the catching of colds, especially winter colds. Sinuses, middle ears, throats, etc., should all be accounted for medically and surgically, and the body be built up through attention to the elements of good hygiene and such aids as codliver oil. If all this succeeds, well and good. But if, as often happens, it does not, then our sovereign resort is to climate.

Climate for this condition means that region where the chances of catching fresh colds are reduced to a minimum. The process is essentially one that is kept stirred up by recurrences of winter colds. Resort to a warm and preferably dry climate is therefore the treatment of choice. In principle, treatment aims at promoting scarring which is to be accomplished mainly by avoiding focal exacerbations activated by acute colds.

Yet even in the ideal warm winter climate, and when fortunately fresh colds are avoided, the infection, once it is well established, does not yield readily. Successful treatment requires months,—of at least the whole of one winter,—and it may take several years. Lacking the irritating effects of fresh colds the patient may become asymptomatic at once and remain so throughout a winter. Yet, as in tuberculosis, exacerbations are possible as long as the process is not completely healed; and once embarked upon the healing of the focus it is a pity to terminate treatment short of this being thoroughly performed, if this is possible. Ideally, it is this accomplishment, and this alone, that should set the term to climatic treatment.

Tetany*

By Jonathan Meakins, *Montreal Canada*

TETANY has been recognized as a clinical entity since the classical description by Clarke in 1815. It appears with great frequency in the older literature but has become of progressively less importance as a distinct symptom complex during the past thirty years. It has been reported in epidemic form in both Europe and America; when it appeared to have a seasonal occurrence particularly in March and April and affected young men between the ages of sixteen and twenty-five, seldom appearing in women.

Like many syndromes of the past, the etiology of which was not understood, it was classified as a distinct disease. It has now been established that 'tetany' is usually only a sign of a more obscure disturbance of metabolism. Where at one time it was considered rather common, its rarity now may be judged by the fact that in the general teaching hospitals attached to the McGill Medical Faculty, out of 219,000 admissions only fifty cases with a primary or secondary diagnosis of tetany were recorded. Of these, thirty-six cases occurred in the Departments of Pediatrics. It is true that a number of instances may not have been recorded, as in recent years the tendency has been to consider it but as a symptom and not as a distinct entity.

Tetany may be defined as "a condition in which the neuro-muscular system exhibits a pathological hyperexcitability to stimuli of normal intensity". The first successful attempt to correlate this condition with a metabolic disturbance was that of MacCallum and Voegtlin[1]. They found in cases of tetany resulting from extirpation of the parathyroid glands that there was a lowering of the blood serum calcium which was in proportion to the severity of the tetanic symptoms. The next important contribution was the demonstration of a low serum calcium and a relatively high serum phosphorus in the tetany associated with rickets. This brought these two well-defined causes of tetany into conformity.

It had long been known that tetany was sometimes associated with pyloric obstruction, gastrectasis and other chronic abdominal conditions which resulted in persistent and long-continued vomiting. But with improved gastro-intestinal diagnosis and surgical therapy these cases became extremely rare. With the introduction of the intensive alkaline treatment of peptic ulcer they re-appeared and it soon was demonstrated that their occurrence depended upon the produc-

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tion of an alkalosis, the blood calcium remaining normal or even being increased. Investigation of the occasional cases of chronic vomiting revealed a similar alkalosis from the excessive loss of hydrochloric acid while an almost identical series of events occured in violent hypernea causing extreme carbon dioxide elimination. The last method produces the most prompt occurrence of tetany due to alkalosis on acount of the ease with which carbonic acid can be removed from the tissues and thus produce a cellular alkalosis. This can be done in a few minutes in comparison to the days which may be required to produce the same degree of alkalosis by the oral administration of alkalies or by vomiting. Even the intravenous injection of alkaline solutions requires some time before tetanic symptoms develop, even though there may be a considerable alkalosis in the plasma. This is explainable on the grounds that the alkaline salts diffuse but slowly into the cells while the removal of carbonic acid from them can be accomplished with great rapidity.

The next class of case, to be elucidated with which tetany is associated, were chronic intestinal disorders,—namely, sprue and allied conditions. Among the other signs of sprue there is a disturbance of the calcium balance with a decrease in the serum calcium. In advanced cases symptoms of tetany develop which may be corrected by the raising of the serum calcium. Blumgart[2] in 1923 reported two cases with chronic diarrhoea and mal-absorption of fat who had tetany while under observation. In one case the serum calcium and serum phosphorus were reported—the former was low, being 5.3 mgms. per cent, while the latter was normal, being 2.6 mgms. per cent. In addition, both cases showed a pronounced reduction in the bicarbonate reserve. In one case where the large bowel was examined, megalocolon was found.

In 1929 Holmes and Starr[3] reported five similar cases of chronic diarrhea, mal-absorption of fat, megalocolon and tetany. In all these cases there was a pronounced decrease in the serum calcium and the tetanic symptoms were only controlled by the use of parathyroid hormone. In none of these cases was the bicarbonate reserve or the pH of the blood reported. There seems no doubt that these cases are closely allied to sprue and that the symptoms of tetany are due to the disturbance of the calcium balance.

Probably the only other condition where there is a distinct reduction in the serum calcium is in chronic nephritis. In many instances this is so low as to warrant the expectation of the appearance of tetany were this a specific cause of the hyper-excitability. The work of Salvesen and Linder[4] and Peters and Eiserson[5] shows that the variation of calcium should not be considered by itself alone but must be interpreted in conjunction with the serum protein and inorganic phosphorus. Peters and Eiserson give the following equation to correlate these three components in the serum—$Ca = -0.255\ P. + 0.566$ protein $+ 7$, and furnish an alignment chart for ready determination of the expected value of one of these if two be known. In the cases of renal disease examined they found that the correlation of these three substances made close agreement when plotted on their chart.

The cases of tetany reported in the present series may be classified as follows:

1) Tetany with rickets and low serum calcium, 36 cases, or 72 per cent.
2) Parathyroid deficiency and low serum calcium, 3 cases, or 6 per cent.
3) Chronic gastro-intestinal disease with fatty stools and low serum calcium, 1 case, or 2 per cent.
4) Excessive alkali intake with alkalosis, 3 cases, or 6 per cent.

In this series no case of true gastric tetany was found. All of those with a past history of peptic ulcer were not vomiting immediately before the onset of the tetanic symptoms but were taking large doses of alkalies.

There are remaining seven cases which do not conform to the usual classification of tetany. One case was admitted with the signs and symptoms of hyperthyroidism and showed definite signs of tetany before operation. The serum calcium at this time was 7.8 mgms. per cent. A sub-total thyroidectomy was done and she made an uninterrupted recovery. Since the operation there has been no return of the tetany although the serum calcium remains at a low normal level, varying between 7.8 and 8.4 mgms. per cent, and all indications of hyper-excitability to mechanical and electrical stimulation have disappeared.

Finally there are six cases which form a group by themselves. These are all women varying in age from 17 to 28 years. In none of them was there any evidence of thyroid, parathyroid, gastric or intestinal disease. In all cases there were the usual signs of tetany—intermittent or continuous rigidity of the muscles of the upper, lower or body extremities, the "accoucheur's hand", or the "main en grippe" was always present. The usual signs of mechanical irritability of neuromuscular systems such as Trousseau's and Chvostek's sign were positive. Some of the spasms were more violent than others and in a number of instances general anesthesia was necessary to remove the painful contractures. The more unusual signs such as strabismus, conjugate deviations of the eyes, contracture of one or both orbicularis oculae, dysphagia, aphonia, laryngeal stridor, explosive vomiting and diarrhea, spasmodic retention of urine, were present in a more or less pronounced degree in all cases. These signs with the altered response to the interrupted and constant electrical current afforded no doubt that these patients were suffering from what is usually considered to be tetany.

There were present, however, none of the usual diseases with which tetany is ordinarily considered to be associated. More intensive study still further failed to reveal any of the usual chemical changes which were to be expected. The examination of the serum showed the calcium phosphorus and protein to be in normal amounts and to have a normal ratio to each other. The basal metabolism was also found to be within normal limits. There was no history of chronic diarrhea, while the stools did not contain an excessive amount of fat.

As all the usual causes of tetany had been explored, attention was then directed to the more unusual causes. It was considered possible that an un-

explained and intermittent alkalosis might have given a clue to the onset of the symptoms, and this was borne out by finding an increased carbon dioxide combining power of the plasma. This ranged in upper limits of normal, being between 65 and 75 cc. volumes per cent; but this was not considered in itself of sufficient magnitude to initiate the symptoms.

There have frequently been recorded cases of so-called hysteria and other psychic disturbances accompanied by respiratory abnormalities and tetany. As to whether these conditions had a definite biochemical foundation has never been fully explored. Likewise in the sequelae of encephalitis lethargica, tachypnea or polypnea associated with tetany has been reported. These cases have still to be investigated from a biochemical point of view.

On further investigation there was found to be in four of the cases here reported a common sequence of events at the initiation of the attacks. They were almost identical in each case. The onset was characterized by an acute pain in the lower sternum or upper epigastrium with a sensation of constriction of the chest. This pain was usually of the most agonizing character and, as the patients all stated, they felt as if their chests were completely filled with air and that they could not expire; this in spite of the fact that laryngeal spasm was present in only one case. The respirations were rapid, ranging between 40 and 60, of a shallow character and at times respirations ceased in complete inspiration. In one case inspiratory apnea occurred over a period of fifteen seconds. After this respiratory pain and abnormal rhythm had continued for a variable length of time tingling in the hands and feet followed by general tetanoid spasms occurred, and the respiratory distress became progresively more severe. In three of the cases a general anesthetic was administered in order to obtain relief of symptoms. In the fourth case the respiratory distress and cyanosis during the initial attack was so alarming, and examination of the larynx appeared to reveal redness and swelling of the larynx, that a tracheotomy was performed. This gave but temporary relief. Unfortunately an estimation of the bicarbonate reserve was not done at this time but subsequently it was found, during an interval between attacks, to be 75 cc. volumes per cent, which indicated a distinct alkalosis. This patient had repeated attacks of respiratory distress each one associated with tetanoid spasms, cyanosis and great apprehension. When she came under our observation we were immediately impressed by the character of the respiratory disturbance. This suggested the probable production of an uncompensated gaseous alkalosis by the polypnea initiated in one who already had a moderate alkalosis. Therefore preparations were made to carry out a therapeutic test as to the probability of this assumption. When an attack was again precipitated by excitement it was allowed to become well established and then the patient was made to inhale a mixture of 5% CO_2 and 95% oxygen. Within a minute the symptoms of tetany completely disappeared although the pain in the lower sternal region still remained. A careful examination at the time of these attacks revealed the fact that abdominal respiration had practically ceased,

that the abdominal muscles were held in a rigid condition and it was surmised that the diaphragm was in a state of tonic contraction. Unfortunately an X-ray examination during an attack was not possible.

It is not suggested that these cases are the after-math of encephalitis lethargica nor that they can be properly classified as hysteria. It seems probable that they are cases of unexplained alkalosis with an unstable nervous control. Whether this instability may be the result of the alkalosis or not is at present not clear but there seems to be a close association between the two conditions. Attempts have been made to institute the attacks by forced breathing; but this so far has been unsuccessful chiefly, we believe, through the resistance of the individuals to undertake real hyperpnea. At no time have we been able to increase the respiratory volume while at rest beyond 8 litres per minute.

It has already been mentioned how easy it is theoretically to produce a cellular alkalosis by increased elimination of carbon dioxide and it is surprising that more cases of tetany due to this cause, independent of those occurring as a sequel of encephalitis lethargica, have not been reported. It is our belief that this is a distinct clinical entity and that after further investigation a definite biochemical explanation is forthcoming. The work of Dale and Evans[6] with excessive pulmonary ventilation producing a rapid removal of carbon dioxide showed that the pH of the blood in dogs could be changed from 7.48 to 7.82 in twenty seconds. Co-incident with this there was a rapid drop of blood pressure which action could be reversed by the same excessive ventilation but using expired air. They demonstrated that this fact was not generally due to the change of pH in the circulating blood but was due to the actual extraction of CO_2 from the tissues, and particularly from the tissues of the central nervous system. We are not inclined to believe that the pH of the blood under all circumstances actually reflects the intra-cellular conditions, and particularly when dealing with such a highly diffusible substance as carbon dioxide.

Up to the present much attention has been paid by clinicians to acidosis and its associated deleterious action on the central nervous system, but as yet little attention has been paid to the opposite disturbance of acid-base equilibrium, namely alkalosis, particularly when resulting from too rapid removal of carbon dioxide. It produces what is commonly known amongst physiologists as an uncompensated gaseous alkalosis,—a condition which is not tolerated by the nervous system and may be fraught with most disastrous results.

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Splenic Puncture as a Diagnostic Procedure in Infancy and Childhood*

By Julius H. Hess, M.D., *Chicago, Ill.*

At no period during life is an enlarged spleen so common a finding as in infancy and childhood. However, emphasis should be placed on the fact that an enlarged spleen frequently does not have the same significance in early life that it does in adults. This applies more especially to the acute splenomegaly of moderate degree as seen during acute infections and the chronic splenomegaly associated with nutritional disturbances.

In a review of the literature numerous classifications of splenomegaly are found, some of them quite complete but none entirely satisfactory from either an etiological, pathological or clinical standpoint. Our limited knowledge of etiologic and pathogenic factors render such a grouping impossible. In this discourse an attempt will be made to formulate a clasification of splenomegalies from the standpoint of the clinical value of splenic puncture as a diagnostic procedure. To properly interpret the material obtained through puncture of the spleen the normal cytology must be established.

From a pathologic consideration the increase in size of the spleen may be due either to hyperplasia of its normal structural elements, the storage of

Classification of Splenomegalies in Childhood from the Standpoint of Splenic Puncture:

I. Splenomegaly Associated with Dysfunction of the Hematopoietic System.
   A. Anemias secondary to defective mineral metabolism.—3
   B. Anemias secondary to defective regeneration (von Jaksch's).—3
   C. Anemias secondary to increased blood destruction.
      1. Hemolytic Icterus, congenital and acquired.
      2. Sickle Cell anemia, as distinguished from sicklemia (Cooley).—5
   D. Purpura Hemorrhagica.—2
   E. Leukemias.—2
II. Splenomegaly Associated with Storage Disorders of the Reticulo-Endothelial System.
   A. Diabetic lipemia.
   B. Niemann-Pick's disease (Lipoid Histiocytosis-Bloom) (Spleno-hepatomegaly-Pick).—7
   C. Gaucher's disease.—7
III. Splenomegaly Secondary to Bacterial and Spirochetal Infections.
IV. Protozoal and Parasitic Splenomegalies.
IV. Protozoal and Parasitic Splenomegalies.

*Read at the meeting of the American College of Physicians, Minneapolis, Minn., February 12, 1930.

abnormal substances or the development of a new tissue which may be inflammatory or neoplastic in nature.

By means of splenic puncture, qualitative changes in the cell structure of the splenic pulp are readily recognized. The interpretation of quantitative changes in both normal and abnormal cells is less definite. Comparative studies of the cellular elements in the circulating blood and the splenic material will aid in clarifying the activity of the spleen in some of the blood dyscrasias.

Cells obtained through splenic puncture can best be evaluated through a conception of—first, cells derived from the normal splenic substances and, second, elements brought to the spleen by the circulating blood.

The splenic substance consists of Malpighian bodies and splenic pulp. The Malpighian bodies are ovoid or spherical structures and comprise a reticulum infiltrated with lymphocytes. In infants and children a lighter central zone can be distinguished. This is composed of large pale cells with large reticular nuclei showing at times active mitotic changes. The cells of the outer zone of the Malpighian bodies show the typical structural characteristics of the mature lymphocytes in that they have a more pyknotic nucleus smaller in size and deeper straining. They also have less cytoplasm than the more centrally situated cells.

The splenic pulp is the tissue proper of the spleen and contains a variety of cells. The cells of the supporting reticulum are large, frequently branched and closely associated with the reticulum fibre. Besides this group, of tissue cell origin, one occasionally encounters cells of the sinus endothelium. Histiocytes (frequently called pulp cells or splenocytes) are found isolated as free macrophages. These cells are endowed with marked phagocytic properties. Under physiological conditions the phagocytosis is directed against worn out erythrocytes but in pathologic processes they may be further concerned in the disposal of bacteria and protozoa and the storage of abnormal products of metabolism.

In addition to the cells above described, cells derived from the circulating blood are also found in the splenic pulp. This is possible because of the unique vascular arrangement of the spleen. The arterial blood instead of passing directly into the veins by the usual capillary connections is allowed to flow freely in the splenic pulp. Thus in the normal splenic pulp we may expect to find erythrocytes, polymorphonuclear leucocytes, lymphocytes, monocytes and blood platelets. While in blood dyscrasias the cells may be representative of changes in the blood forming organs.

Technic of Splenic Puncture

In the presence of a large spleen it can be performed without difficulty. With the patient in a recumbent position, the spleen is held firmly against the abdominal wall with the left hand. In children a needle about 3 cm. in length, attached to a well ground 2 or 5 c.c. glass syringe is used. We have found a 22 gauge needle with a blunt bevel most satisfactory as with such a fine needle there is less danger of hemorrhage. In young children at least a partial anesthesia or the use of sedatives is recommended, because of

the danger of tearing the spleen in a struggling child. Only moderate suction should be used. The plunger should not be released until the needle is withdrawn, otherwise the splenic content will be lost through return of the piston by the negative pressure created. Under no circumstances should more more than a few drops be withdrawn. Following puncture 0.2—0.3 cc. of 1-1000 adrenalin solution should be injected subcutaneously. This causes contraction of the splenic capsule. Splenic puncture is contraindicated in the presence of prolonged bleeding or coagulation time.

Staining the Splenic Smear

The combined May-Grünwald-Giemsa has been used for our staining. In addition brilliant cresyl blue was used to emphasize the reticulation of the red cell.

Classification of Splenomegalies in Childhood From the Standpoint of Splenic Puncture:

I. *Splenomegaly Associated With Dysfunction of the Hematopoietic System.*

A. Anemias secondary to defective mineral metabolism.

Insufficient mineral deposits may result from a deficient iron intake or insufficient utilization as seen in simple nutritional disorders. These factors may account for the anemias with splenomegaly present in many cases of rickets.

In both these types there is only moderate splenic enlargement. Splen-

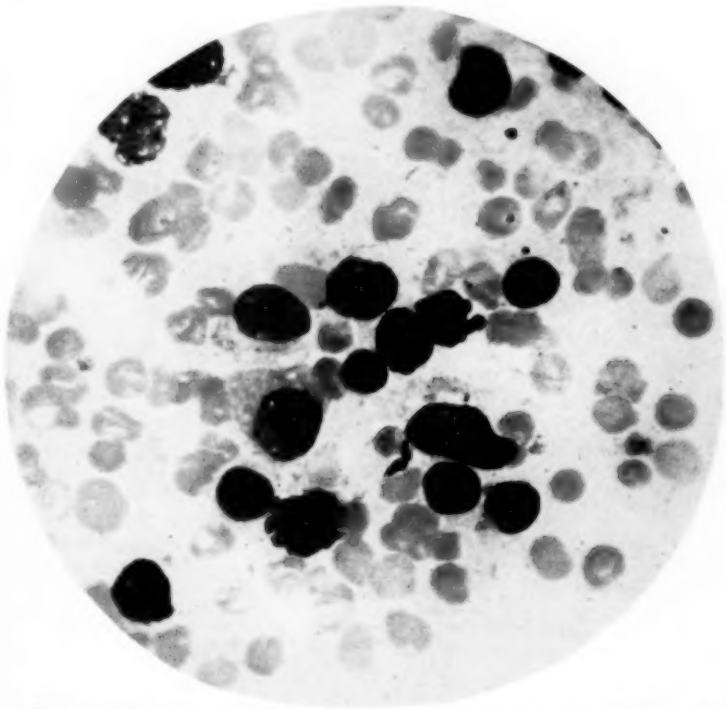

Fig. 1. Stanley M., age 14 months. Splenic puncture—Normal cytology of the splenic pulp. Reticulum cells, lymphocytes, red blood cells.

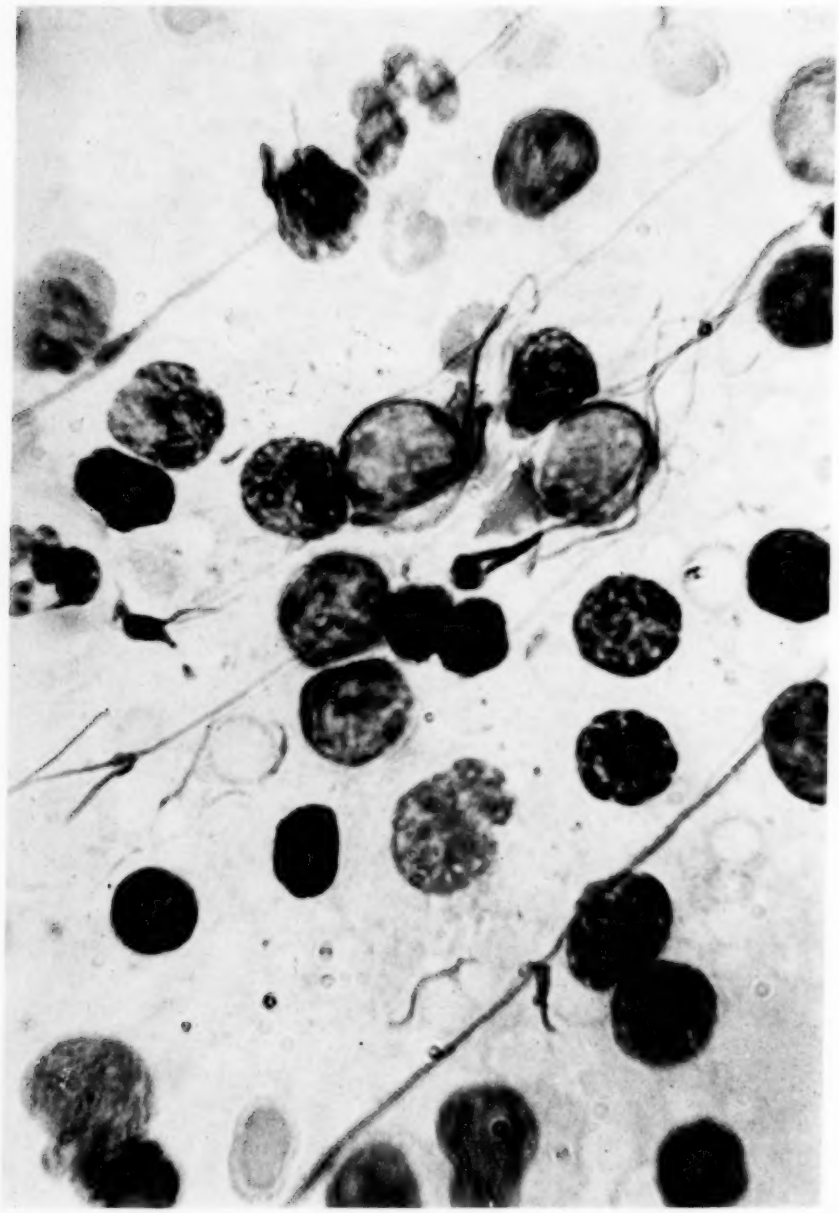

FIG. 2. Bernice M., age 18 months. Splenic puncture—marked rickets with anemia and splenomegaly. Normal cytology with increase in reticulum cells showing reticulum fibres and lymphocytes.

ic puncture is unwarranted as clinical examination and study of the peripheral blood reveals a picture sufficiently characteristic for diagnosis.

B. Anemias secondary to defective regeneration.

Under the stress of very severe chronic anemias in infancy and childhood, changes are often found in organs which, during fetal life, took part in the formation of erythrocytes. Where a marked anemia has persisted for a long time or where there has been an extensive injury to the bone marrow, post mortem studies have revealed numerous erythroblasts, myeloblasts, myelocytes and other primitive cells in the splenic pulp such as are seen in actively regenerating bone marrow. Evidence of this reversion to myeloid function may be obtained by splenic puncture during life.

The nature of von Jaksch's anemia is obscure, though the majority of the investigators agree that it is closely related to secondary anemias and represents a characteristic response of the infantile hematopoietic system to stimulation rather than an independent disease. The fact that cases of von Jaksch's anemia have successfully been treated by splenectomy throws some doubt as to

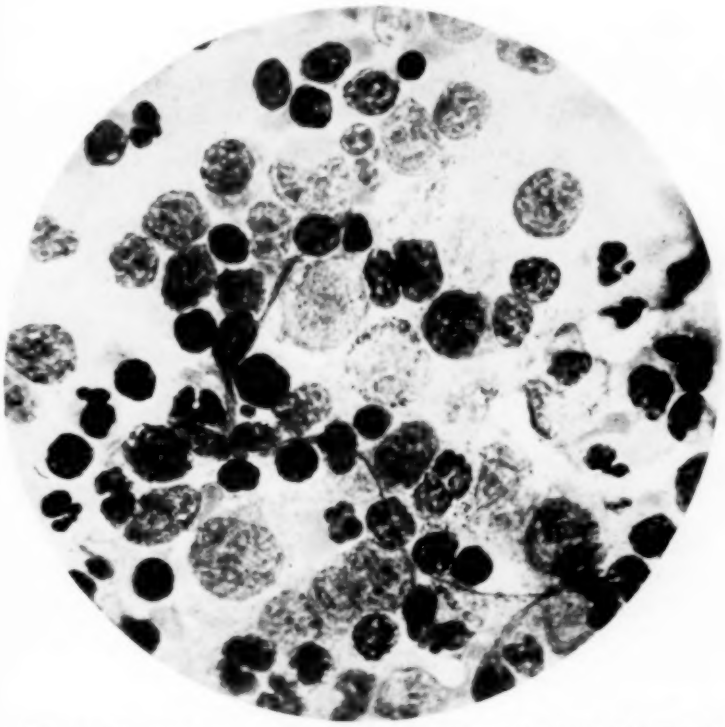

FIG. 3. Thomas K., age 10 months. Splenic puncture Von Jaksch's anemia—marked myeloid metaplasia with granulocytes and red cells in all stages of development.

whether the spleen itself is the seat of metaplasia in at least some of the reported cases.

C. Anemias secondary to increased blood destruction.

Clinical and pathologic evidence supports the current opinion that the spleen plays an important part in the destruction of the red cell. Where this function is hyperactive one encounters splenomegaly, usually of a moderate degree.

Typical of the hemolytic anemias are:

1. Hemolytic Icterus, congenital and acquired. Splenic puncture is not indicated as clinical and laboratory examinations will reveal the nature of the condition.
2. Sickle Cell Anemia, as distinguished from sicklemia. (Cooley).

Reported cases of Sickle Cell Anemia show that splenomegaly is an inconstant finding. (15%). It is more than likely that at some stage of the disease splenomegaly is present. In most instances even in the presence of an enlarged spleen examination of wet sealed preparations of the peripheral blood is sufficient for diagnosis. Allowing the blood to stand suspended in a physiological anticoagulent, in a sealed preparation, tends to induce the sickling phenomenon when it is not present spontaneously. It may be necessary to make repeated examinations and observe the blood for as long as 24 hours as the phenomenon is inconstant.

In the case illustrated above in Figures 4, 5, and 6, the stained preparations of the peripheral blood showed marked erythropoiesis, reticulocytosis (40%) and monocytosis (36%). The presence of marked numbers of nucleated red cells in a child of this age would suggest von Jaksch's syndrome but the large numbers of reticulocytes and monocytes are not often associated in that condition. As none of the clinical characteristics reported in cases of Sickle Cell Anemia were found, the presence of splenomegaly in conjunction with the blood picture might have suggested a blood dyscrasia. Splenic puncture, however, established the diagnosis.

D. Purpura Hemorrhagica.

While a study of the thrombocytes in the peripheral blood, the bleeding time, coagulation time and clot retraction time gives sufficient evidence for gross diagnosis it does not differentiate the underlying pathology.

In a consideration of thrombocytopenia it is important to know whether there is an insufficient new formation of the platelets in the bone marrow due to an alteration of the stem cells of the platelets, the megakaryocytes (Wright), as seen in aplastic anemia, or, on the other hand, increased retention and destruction due to thrombocytolytic action of the spleen. It is in the latter form that splenectomy is of therapeutic benefit.

While splenic puncture might differentiate the nature of the pathologic process, the character

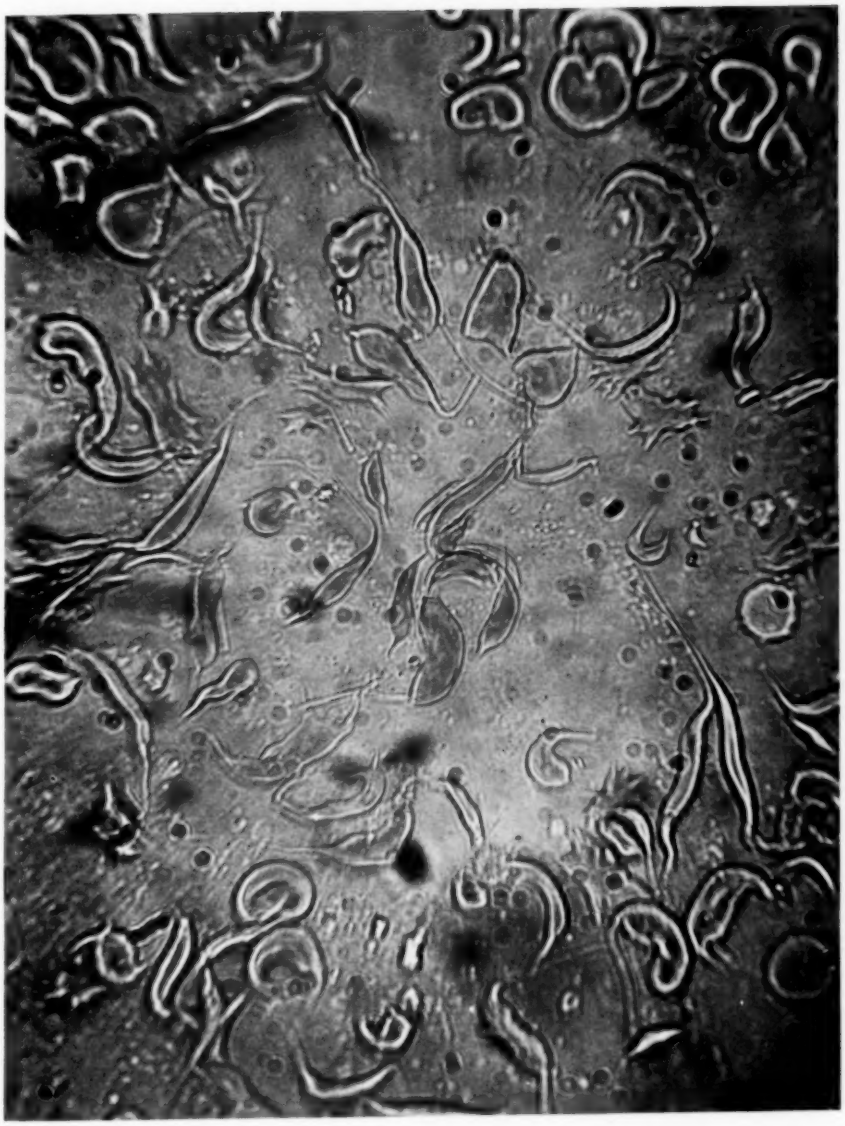

FIG. 4. Baby W. G., age 2½ years. Splenic puncture Sickle Cell Anemia. Fresh unstained specimen.

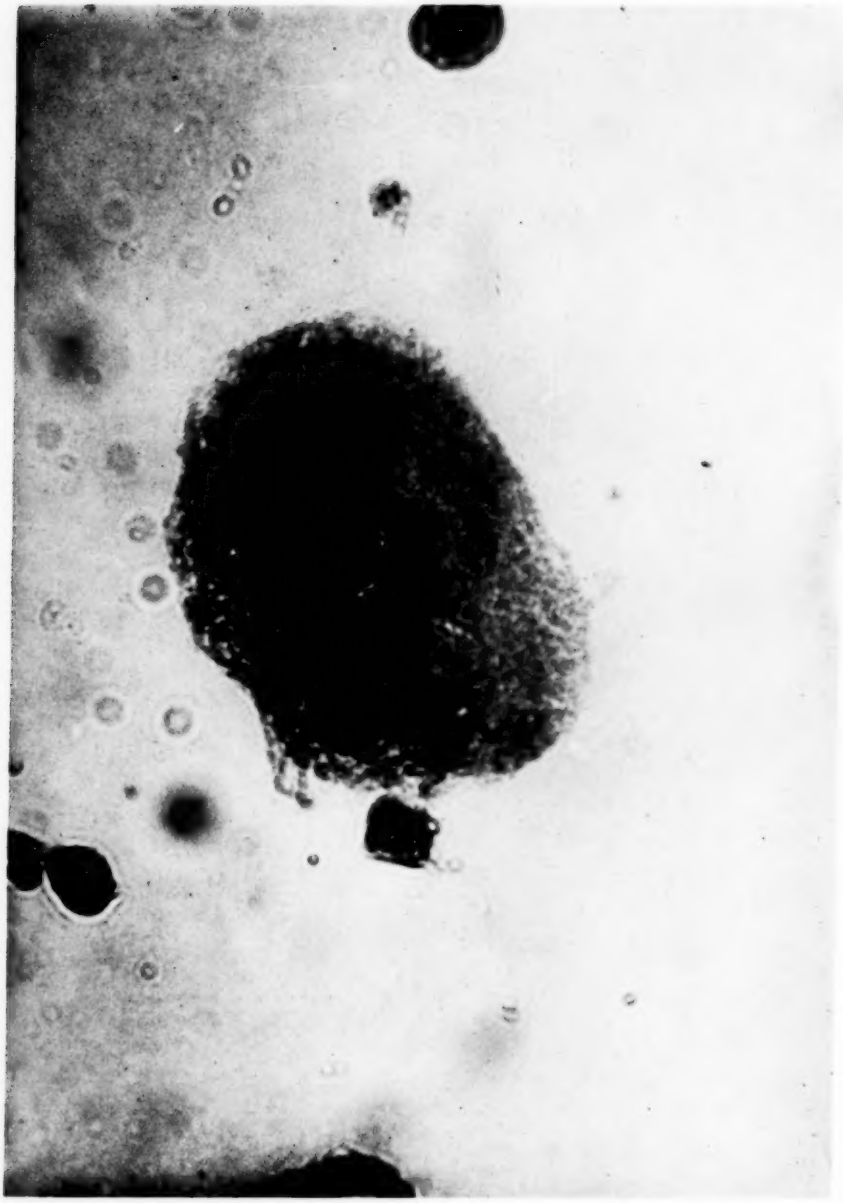

FIG. 5. Baby W. G., age 2½ years. Splenic puncture Sickle Cell Anemia. Histiocyte with an engulfed elliptical red cell.

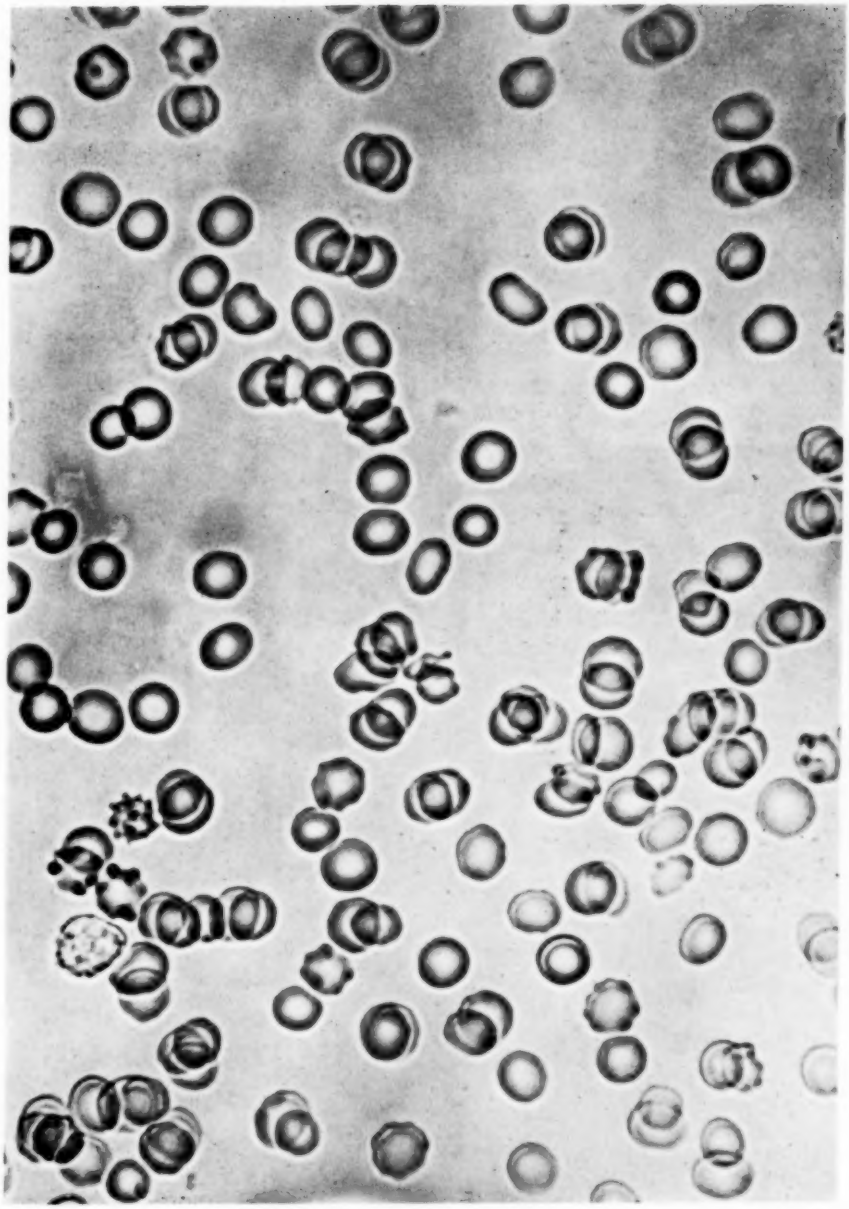

FIG. 6. Baby W. G., age 2½ years. Peripheral blood Sickle Cell Anemia shows no sickle cells after having stood one hour as a wet sealed preparation.

of the disease in most cases would preclude splenic puncture. This is specifically true in acute cases in which an etiologic diagnosis between purpura hemorrhagica and conditions secondary to infection has not been established.

This case made an uneventful recovery after splenectomy and one year later remains in good health.

E. Leukemias.

In no other blood dyscrasia is the departure from the normal blood picture more striking than in typical cases of leukemia. However, much difficulty may be encountered in the aleukemic types or stages. Here splenic puncture may be of value.

Splenic puncture is contra-indicated in acute processes of leukemia when the platelet count is low.

II. *Splenomegaly Associated with Storage Disorders of the Reticulo-Endothelial System.*

Even under normal conditions various lipoids may at times be stored in the reticulo-endothelial cells of the spleen. In certain cases with hypercholesterolemia and lipemia enlargement of the spleen is due to extensive proliferation of cells derived from the reticulo-endothelial system. The relationship of spleen to cholesterol metabolism was established by the work of Anitschkow, who produced infiltration of these phagocytic cells with high cholesterol feedings in rabbits.

A. Diabetic lipemia.

In the lipemia of diabetes splenomegaly is not uncommon. The spleen becomes infiltrated with foam cells which cytologically and micro-chemically produce a picture quite similar to that of Niemann-Pick's disease. Splenic

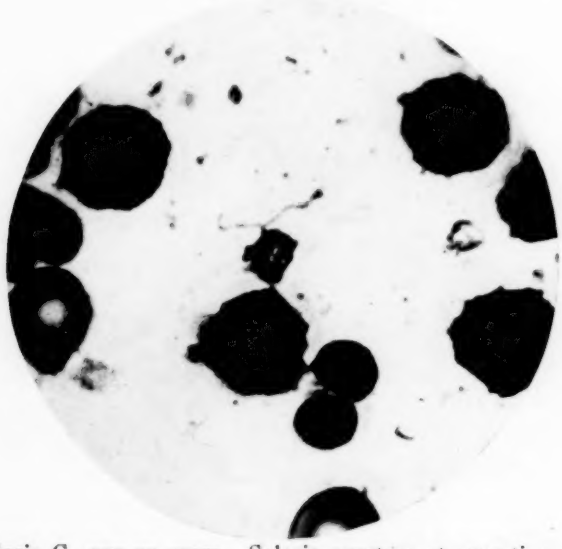

FIG. 7. Marjorie C., age 10 years. Splenic puncture at operation. Purpura hemorrhagica—many platelets present—megathrombocyte in process of throwing out fibrin. Blood showed only 3000 platelets per cm.

puncture is seldom indicated here as the underlying cause of this type of splenomegaly lends itself to clinical recognition.

B. Niemann-Pick's disease (Lipoid Histiocytosis-Bloom). (Spleno-hepatomegaly-Pick).

The Niemann-Pick disease is characterized by early age of onset, its rapid course and early fatal termination. There appears to be a special predilection for the Jewish race. Many of the reported cases have shown the typical clinical manifestations and fundus changes of amaurotic family idiocy. Mental and physical deterioration is frequently found. The skin usually presents a greyish-yellow color with the occasional occurrence of Mongolian spots.

This disease is characterized anatomically by the presence of large, so-called "foam cells". These cells are not limited in their distribution to the reticulo-endothelial system, but are also found

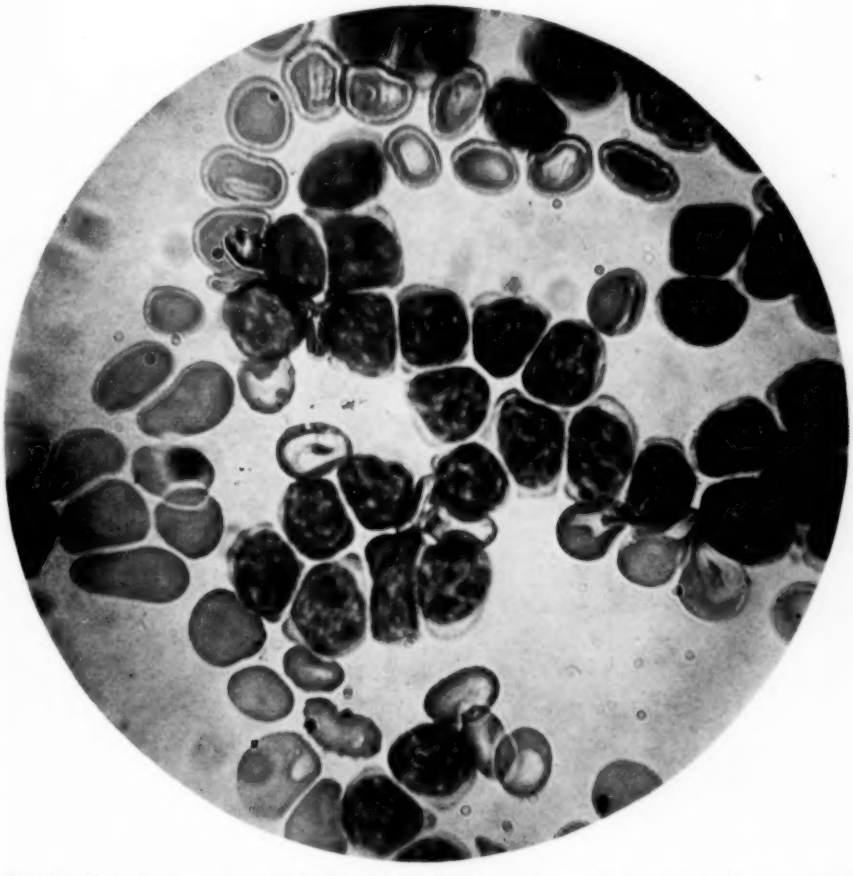

FIG. 8. Splenic puncture aleukemic leukemia 800 white cells per cm. of blood. Splenic puncture specimen showed more lymphocytes than red cells.

in the parenchymal cells of various organs. All organs and tissues may be involved. The spleen becomes greatly enlarged—in the reported cases it varied from 62 to 480 grams, as compared with an average normal size of 30 grams in infants between the first and second years. Pathologically, one finds the picture resulting from the extensive deposition of lipoids in the cells of the various organs.

C. Gaucher's disease.

Aside from the striking clinical differences, mainly of age and chronicity, which it shows in comparison with Niemann-Pick's disease, it is to be differentiated anatomically from the latter in that the typical cells, except in very rare instances, are limited to the spleen, liver, lymph nodes and bone marrow. The spleen becomes enormously hypertrophied. In the spleen the sinuses, as well as the pulp are involved—in the liver the periportal connective tissue is chiefly involved—in the lymph nodes and bone marrow the changes are in the reticulum cells. Cytologically the large cell in Gaucher's disease has a characteristic longitudinal striation with Mallory's aniline blue. Many are multinuclear with the nuclei eccentrically situated.

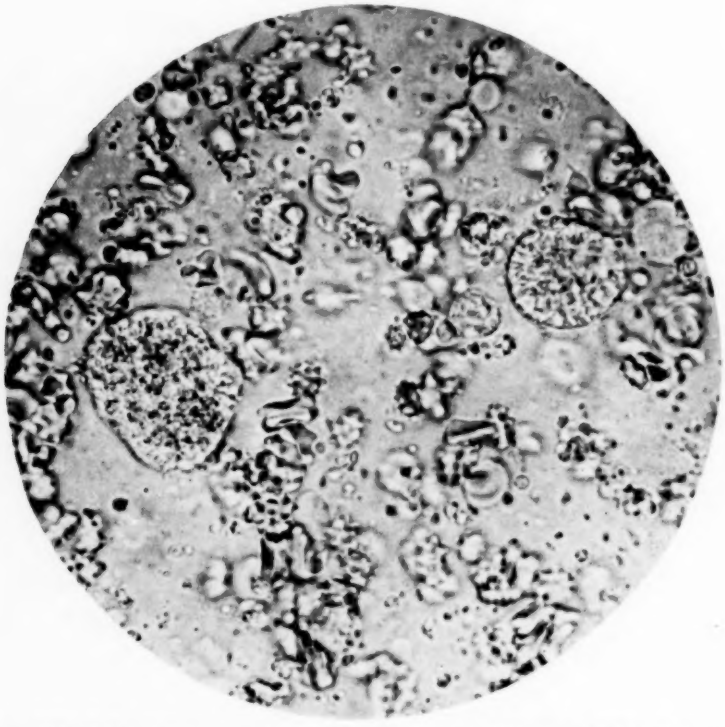

FIG. 9. Alfred S., age 11 months. Splenic puncture Niemann-Pick's disease—showing histiocytes infiltrated with lipoid material (foam cells). (X 900).

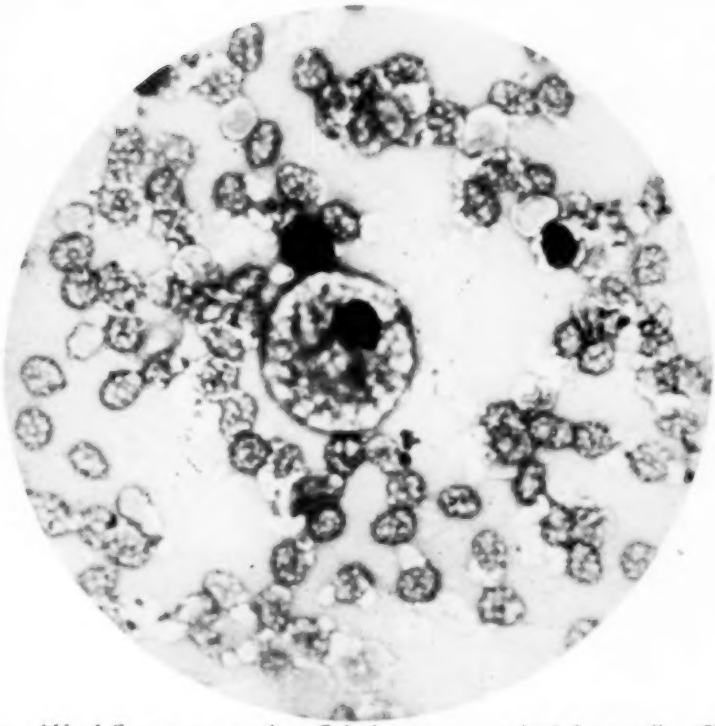

FIG. 10. Alfred S., age 11 months. Splenic puncture stained foam cell. (X 900).

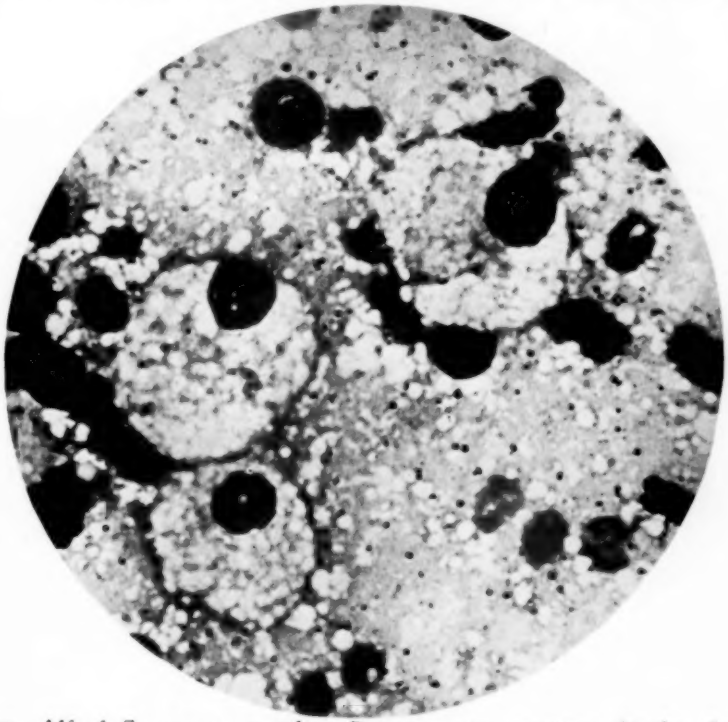

FIG. 11. Alfred S., age 11 months. Bone marrow puncture, showing foam cells stained. (X 900).

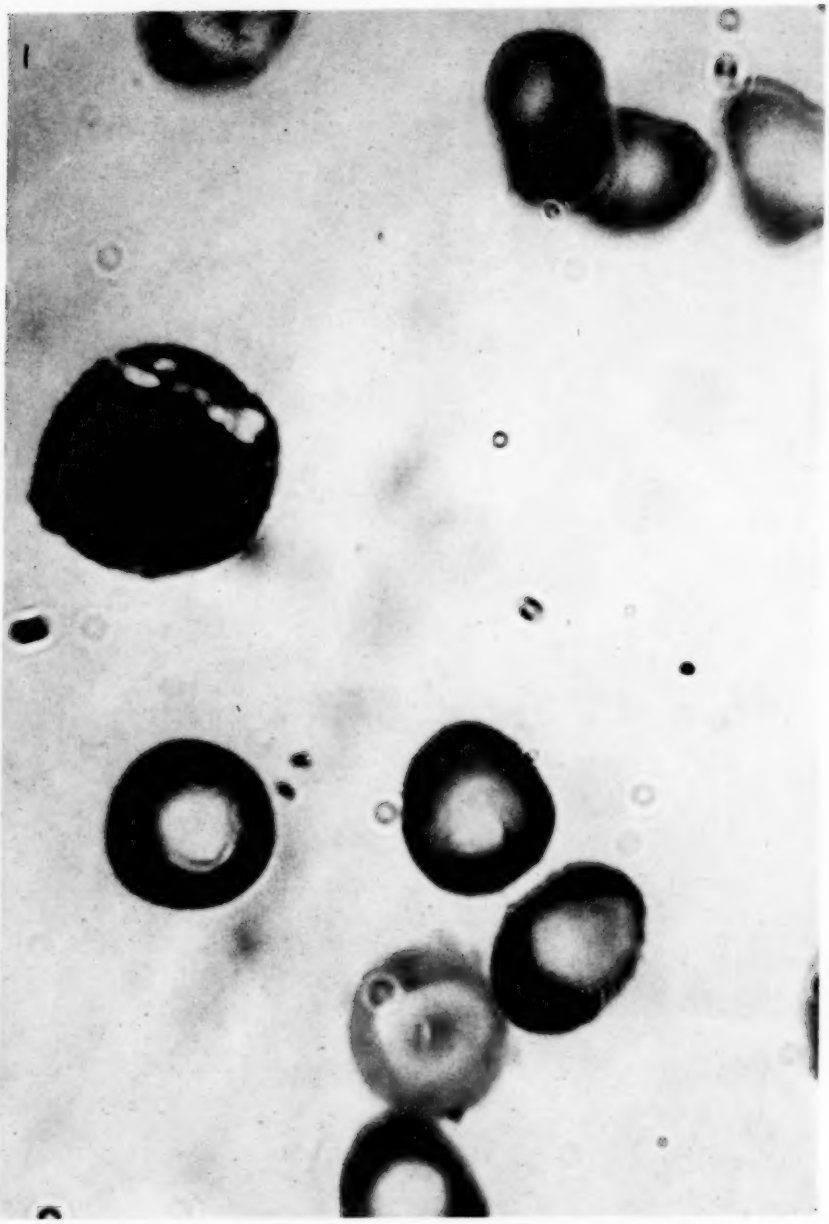

FIG. 12. Alfred S., age 11 months. Peripheral blood smear showing vacuolization of a lymphocyte. (X 2400).

The stored material in Gaucher's disease has been described as a complex nitrogenous substance to which the name kerasin has been applied. This according to all chemical studies is not cholesterin or lipoid.

Gaucher's disease begins insidiously in infancy or childhood, usually before the thirteenth year, and pursues a very chronic course. The enlargement of the spleen, which may reach enormous proportions, is sometimes discovered accidentally or as the result of local symptoms, or else the anemia with its train of symptoms may be the first to become apparent.

III. *Splenomegaly Secondary To Bacterial and Spirochetal Infections.*

Splenic puncture is only exceptionally indicated as a diagnostic procedure.

In atypical cases of tuberculosis, typhoid fever, syphilis, relapsing fever and other infections, it has been practiced without harmful results. The element of danger should, however, be given due consideration in every case.

IV. *Protozoal and Parasitic Splenomegalies.*

Malaria. Splenic puncture, while only exceptionally necessary to a diagnosis, may be the only method by which it can be confirmed. In the absence of plasmodia the finding of histiocytes filled with the dark brown

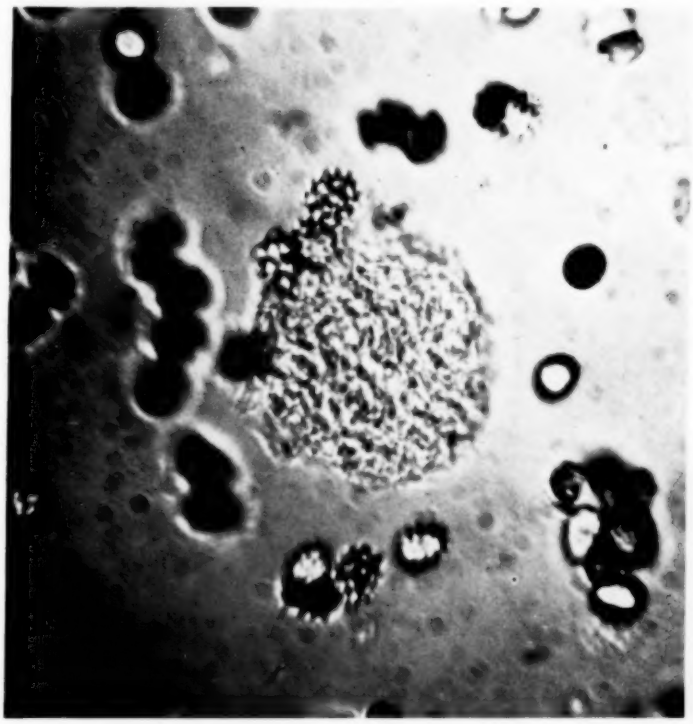

FIG. 13. Langford, age 17 months. Splenic puncture—fresh unstained Gaucher's cell showing typical fibrillar appearance.

granules of malaria pigment is suggestive.

Tropical Diseases. Splenic puncture has repeatedly been used to isolate the parasites of Kala-azar and sleeping sickness.

In the presence of cysts of the spleen, as seen in ecchinococcus infection, it should be considered as a dangerous procedure.

V. *Tumors of the Spleen.*

In hemangiomas, cysts and malignant tumors it is contra-indicated.

Summary

In summarizing, it may be stated that splenic puncture may be of value in substantiating the diganosis of anemias secondary to defective regeneration, such as von Jaksch's syndrome, in subacute and chronic cases of aleukemic types of myelogenous and lymphatic leukemias, Niemann-Pick's disease, Gaucher's disease and exceptional cases of bacterial and protozoal splenomegalies.

Splenic puncture is contra-indicated in the symptomatic purpuras, hemophila, acute bacterial infections and in tumors of the spleen due to hemangiomas, cysts and malignant tumors. Puncture of the spleen should not be attempted in any case where the bleeding or clotting time is prolonged.

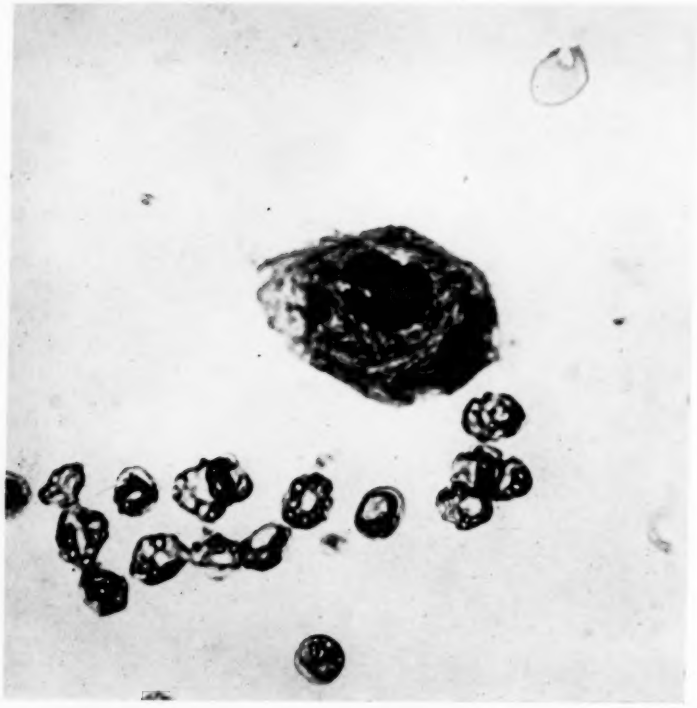

Fig. 14. Langford, age 17 months. Splenic puncture—stained preparation of Gaucher's cell showing fibrillar structure and necleus.

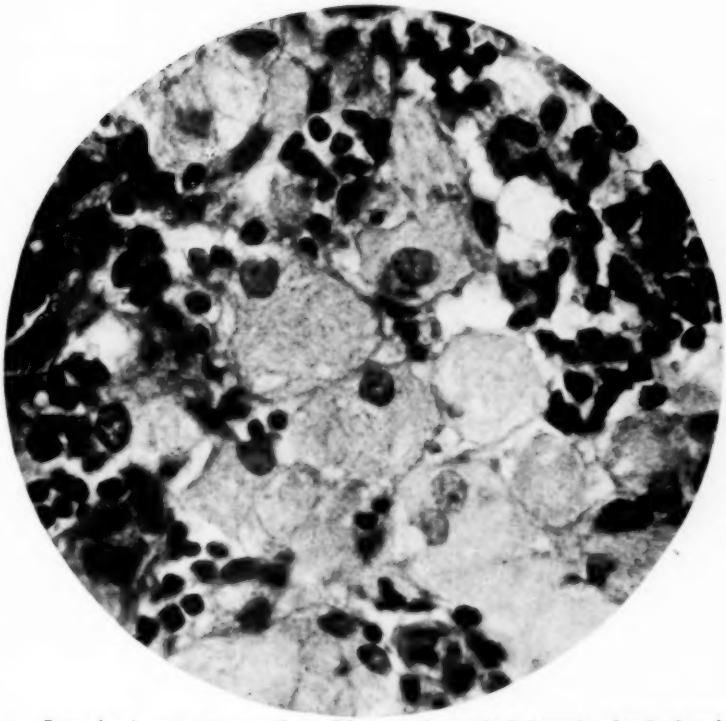

FIG. 15. Langford, age 17 months. Biopsy of cervical lymph gland showing typical Gaucher's cells.

Undulant Fever in California*†

By J. Edward Harbinson, M.D., *Woodland, California*

Undulant fever has received considerable attention in the medical literature, especially since the notable discovery by Alice Evans[1] of the relationship of the Micrococcus melitensis of Bruce to the Bacillus abortus of Bang. There are still many unsolved problems relative to this disease and, in our present formative stage of investigation, we should hesitate to draw conclusions from presumptive evidence.

Incidence in United States: About 1500 cases[2] have been reported in the United States during the past three years. It is the opinion of the United States Public Health Service[3] that undulant fever is not so prevalent in this country as to constitute a major health problem.

Incidence in California:..The disease was made reportable in California in July, 1927. From this date to January, 1930, ninety-seven cases have been recorded. There is a striking difference in the number of cases listed by years. From July to December, 1927, fifteen cases were reported; the following year there were eleven; and during 1929 there were seventy-one. The morbidity rate for 1929 in California was 1.59 per 100,000 population. The typhoid morbidity rate was 13.6 per 100,000 for the same year. The marked increase in the number of cases reported during 1929 may be explained in part by recent publicity given the disease by the medical and lay press. In addition, criteria for diagnosis of Brucella abortus infection are only lately being recognized by the general practitioner. As already emphasized in the literature, the incidence of undulant fever in a given community may be proportional to the efforts and earnestness of the physicians in determining its prevalence. The progressive increase in the number of cases reported in California suggests an increased incidence.

Approximately 45 per cent of the cases were reported from Los Angeles County. Possible explanations for this large percentage are: available laboratory service through eleven district units of the county health service permitting a larger number of serums to be tested in suspicious cases; close proximity to Arizona, New Mexico and Texas, with possible introduction of more virulent strains of brucella organisms from these states; considerable medical and lay publicity in regard to the signs and symptoms of the disease.

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*Read before the meeting of the American College of Physicians, Minneapolis, Minn., February 13, 1930.

†From Department of Medicine, Woodland Clinic.

Age and Sex Incidence:. Two-thirds of the patients were 25 years of age or older. The greatest number were in the age group from 25 to 34. The sex incidence was: fifty-nine males and thirty-eight females.

Occupational and Regional Distribution: The occupations of the majority of the patients did not bring them in contact with livestock or with meat products. Most of them lived in towns or cities; a small percentage of them lived on farms.

Incubation period: The onset of the disease usually was insidious, and often many incorrect preliminary diagnoses were made. The incubation period in one patient who aspirated antigen was twelve days. The usual incubation period is estimated as ten to fifteen days. The time from the onset of symptoms to the date of diagnosis varied from a few days to a year.

Symptoms and Findings: The temperature was surprisingly high in relation to the pulse, appearance and general condition. Patients with a fever of 101 to 103 degrees had pulse rates of only 90 to 100 and respirations of 20. The pulse rate often was not over 115 with a temperature of 105.5.

The clinical findings were those which are commonly found in any type of bacteremia. The chief complaints were often misleading. One woman complained only of dysmenorrhea and nervousness. The most frequent symptome were: weakness, general malaise, fever, headache, sweats, chills or chilliness, abdominal pain and distress, anorexia, aching pains in muscles, bones or joints, weight loss of from 10 to 50 pounds, and irregularity of bowel function—usually constipation, but occasionally diarrhoea. Less frequent symptoms were: nausea, vomiting, dizziness, cough, sore throat, sore gums or teeth, and catarrh. The symptoms, including fever, were usually more pronounced during the late afternoon and night. The temperature curve was more of a continuous type, with slight undulations, in most of the cases; in a few it was the typical undulatory type. It was not always possible to tell how a patient was feeling on any particular day by looking at his temperature chart as the severity of the symptoms did not always follow pari passu the temperature curve. One patient with a nightly temperature of 104 to 105 degrees had no chills and only very mild sweats. His only complaint was backache and he insisted on returning to work.

Physical findings: The outstanding physical finding was an enlarged spleen. Other occasional findings were enlargement of the superficial lymph glands and enlargement of the liver. Skin manifestations varied from small crops of petechiae to erythema nodosum-like lesions. Localization of the infection gave rise to such complications as prostatitis, epididymitis, pelvic disorders, optic neuritis and cellulitis. The clinical picture was usually suggestive enough to warrant a blood test for the presence of brucella agglutinins. Most of the cases correspond to the intermittent variety of the disease. Symptoms usually disappeared after subsidence of the fever and the spleen decreased to normal size. The length of illness

varied from three weeks to eighteen months. Relapses were infrequent.

Differential diagnosis: Undulant fever is most frequently erroneously diagnosed as: typhoid, malaria, influenza, tuberculosis and arthritis; less frequently as: sinusitis, endocarditis and paratyphoid. Patients may be subjected to laparotomy on account of severe abdominal pain. Certain predominant symptoms or complications may prompt the patient to consult specialists. Thus the gynecologist may be the first to see undulant fever patients for pelvic complaints, the genito-urinary specialist may be consulted for urinary complications and the orthopedist on account of joint pains.

Atypical Cases: The atypical cases are often overlooked. One patient complained only of pruritus, and, on examination, acarus scabiei was found. He mentioned no other symptoms. Ordinarily this patient would have been given appropriate home treatment for this disease and his temperature probably would not have been taken. In this instance he was sent into the hospital and his temperature record showed a fever of 102. His occupation—that of milker— aroused a suspicion of undulant fever and, on questioning, he gave a suggestive history of the disease. Laboratory tests confirmed the diagnosis.

In a recent survey, a blood sample was taken from a man who had charge of an isolated herd of positive reactors. Brucella organisms had been isolated from the milk of these cows and recently there had been several abortions among the herd. The patient's duties included the care of the cows at these times. He had drunk only pasteurized milk during the past one and a half years. He did not consider himself sick and probably would not have consulted a physician. He was doing his work in the usual manner. After routine questioning, we obtained a history which suggested that the infection had been present for about six weeks. His spleen was palpable and he had a fever of 102 degrees. An agglutination test was positive for Brucella abortus "80" in a dilution of 1:5120. Brucella abortus bovinus was recovered from his blood.

These are the types of cases of undulant fever which usually are overlooked.

Laboratory tests: The average red blood cell count in this series was 4,400,000 with a hemoglobin average of 70. These figures are somewhat higher than those reported by other investigators. The white blood count varied from 3,500 to 14,500 with an average of 6,000. The polymorphonuclear average was 59 and the lymphocytes 31.

No laboratory procedure is comparable to recovery by culture of the brucella organisms from the blood, urine, feces, or a localized infection. Apparently the organism may remain viable in the body for years and may be recovered from the site of localization even though the agglutination test of the blood is negative.

From the patients reported from California, only three positive blood cultures were obtained. Two patients contracted their infections in the vicinity of Phoenix, Arizona, and the organisms recovered were Brucella melitensis. They were isolated by Dr.

Karl Meyer of the Hooper Foundation. We have obtained only one positive culture as already mentioned.

The agglutination test is probably the next most valuable laboratory aid. The procedure is essentially the same as a Widal test, except that brucella antigens are used, the strain most commonly employed being Brucella abortus 80 and Brucella melitensis 428.

Most laboratories report an agglutination titer of 1:160 or higher as positive. Lower positive titers excite suspicion and call for investigation by the clinician.

The presence of brucella agglutinins in the blood does not necessarily imply that the individual is suffering from active undulant fever. An agglutination titer of 1:1280[4] was found in an individual who was perfectly well and who denied any previous illness suggestive of undulant fever.

Very low agglutinations of 1:15, 1:30[5] are found occasionally in patients with severe undulant fever. A few patients with positive cultures have shown no agglutinins in their blood..[5] It should be emphasized strongly that positive agglutination tests alone should not be considered sufficient evidence for a diagnosis of undulant fever. The clinician must exercise his judgment in each case and render his diagnosis according to the mass of clinical and laboratory evidence for or against the presence of the infection. It is important that all dilutions up to 1-1280 be tested on account of the pre-zone phenomena. In Keefer's case[6] the agglutination was 1:20,000 with no agglutination up to 1:1200. The agglutination titers in this series varied from 1:80 to 1:10,240, with an average titer of about 1:1280.

In some cases agglutinins rapidly disappeared from the blood while in others relatively high titers were obtained a year or more after subsidence of symptoms. Birt and Lamb[7] have reported the presence of agglutinins in the blood of a patient seven years after recovery from the disease.

Some patients with high titers were not very sick; others with low titers had severe symptoms and vice versa. Graphs of the agglutination titers were not valuable in estimating the length or severity of the illness or the prognosis.

In Europe, both agglutination and complement fixation tests have been done on suspected cases. The blood of one of Loeffler's[8] patients showed complement fixation and on agglutinins. King[9] has been able to get complement fixation in many cass before he could demonstrate agglutinins.

The skin test may prove to be a valuable diagnostic procedure. Meyer[10] and his associates were the first to introduce this test and at present are experimenting with a purified abortus protein.

Other experimenters have used both filtrates (three weeks old)[11,12] and heat killed suspensions of the organisms in salt solution[13,14]. Giordano[15] has used the latter preparation and reports good results but rather severe reactions.

The problem of bacteriological differentiations of the varieties of the brucella group is still unsettled. Absorption tests, if reciprocal, are valu-

able. Absorption tests on serum alone are not reliable. The dye differentiation test may be valuable but Meyer[16] has noted that certain dyes give contradictory results.

The guinea pig test may give valuable leads, but is not absolutely dependable. The pathogenicity tests on monkeys with recently isolated strains may classify the bovine and the porcine strains, but not the melitensis.

Carpenter[17] has recovered both typhoid bacilli and Brucella abortus from the blood of one patient; Giugni and Savorini[18] observed a combination of malaria and Malta fever.

During 1929, the California State Bacteriology Laboratory examined 156 blood specimens that had been sent in for the Widal test and found that five of these gave a positive agglutination with abortus antigen. It also received 164 blood specimens on which examinations for abortus agglutinins were requested. Twenty-three of these were positive, 137 were negative and four were doubtful positive (1:40 dilution).

Tests of six individuals working in one laboratory devoted almost exclusively to brucella research work showed four positive reactors. Half of the workers in another laboratory doing the same type of work showed positive agglutinins in their blood. Of all these workers, only two had definite symptoms of undulant fever.

Many serums were tested for cross agglutination with Bacterium tularensis but none were found positive.

Brucella infections as a cause of abortion in women: We have tested the serums of twenty-five women who have repeatedly aborted. The agglutination test was positive in low dilutions of two of these serums. The past history of one women was very suggestive of previous undulant fever.

Carpenter[19] examined blood samples from twenty-eight women who aborted and made bacteriological studies on twenty-seven fetuses and twenty-eight placentas. In thirteen cases the placenta and fetus were from the same case, making forty-two abortions from which material was examined. Abortions ranged from thirty days to the seventh month of pregnancy. There was no evidence that Brucella abortus was the cause of the interrupted pregnancies.

Simpson[20] reports an agglutination titer range from 1:80 to 1:329 for five women who repeatedly aborted. Four of these women gave history of a previous febrile illness. All consumed raw milk.

Cornell[21] examined the serums of 1015 women reporting to the prenatal clinics of Chicago Lying-in and Cook County Hospitals. Five serums gave weakly positive reactions. None of these patients gave any suggestive history of undulant fever and, clinically, there were no premature interruptions of pregnancies. Two of the patients were delivered of normal children at full term. Twenty-three cases of abortions in women were studied: twenty-two patients were negative and one gave a weakly positive reaction with placental blood. The venous blood was negative.

Kristensen[22] isolated Brucella abortus from the exudate which covered the uterine site of the placenta in a seven months fetus. No organisms

were isolated from the stomach, intestine, lungs, liver, spleen or kidneys of the fetus.

Frei[23] isolated brucella organisms from the vaginal discharge of a woman ten days after the onset of symptoms.

Treatment of Undulant Fever: Many types of treatment have been used, but, in our experience, none has been so uniformly successful as vaccine. The best results have been obtained when the dosage was sufficiently large to produce a febrile reaction of 2 to 4 degrees. We have used a sensitized mono-bacterial vaccine prepared from a human abortus strain. The initial injection was ¼ cc. Injections were given every day, doubling the amount of vaccine given on each occasion. Suitable febrile reactions usually were obtained with 1 to 2 cc. of the vaccine. Vaccine contained 1,000,000,000 organisms per cc.

Deaths: There were two deaths among the ninety-seven patients reported in this series. One of them had suffered from endocarditis and myocarditis for many years prior to the onset of undulant fever. He did not have the malignant type of the disease. A post mortem examination of this patient was permitted and the following findings recorded:

Numerous petchiae on the back and scattered over the upper arms and chest.

Lungs: Broncho-pneumonia; chronic passive congestion all lobes of both lungs; hemorrhagic tracheo-bronchitis and lymphadenitis.

Heart: Weighed 420 grams; marked hypertrophy of right ventricle; large vegetation present on the mitral valve, extending onto the under surface of the aortic cusp.

Spleen: Weighed 470 grams; large and flabby; cut surface light red.

Liver: Weight, 2,725 grams; capsule smooth, but with a mottled appearance; cut surface showed chronic passive congestion with patches of marked parenchymatous degeneration.

Gastrointestinal Tract: Upper part of esophagus and larynx congested; vessels prominent, but no bleeding points found; stomach mucosa comewhat congested; no pathological change found in small or large intestine.

Microscopic Examination: *Heart*: Several masses of perivascular exudate consisting of large mononuclears, lymphocytes and a few polymorphonuclears.

Tracheal Lymph Node: Congested; sinuses filled with blood and exudate; number of polymorphonuclears, endothelial cells; some edema and hazing of architecture.

Bronchial Lymph Node: Same picture, but exudate was more mononuclear.

Testicle: Not remarkable.

Spleen: Capsule slightly fibrosed; considerable blood in pulp; splotches of hyalin in follicles, which looked like amyloid; media of the follicular arteries also showed considerable of this material; pulp showed marked hyperplasia polymorphonuclears.

Liver: Marked central congestion with almost complete destruction of central parenchymal cells and invasion of polymorphonuclears; considerable fat in remaining liver cells, in small droplets; occasional excess of exudate in periportal tissue, mostly small mono-

nuclears, few large polymorphonuclears.

Methylene blue stains of lung and lymph nodes failed to reveal any gram negative bacteria.

Cultures were made from heart blood and spleen on blood agar plates and in broth.

Guinea pigs were inoculated with splenic material but showed no effects in ten weeks. Serum from the guinea pigs did not agglutinate Brucella melitensis.

Postmortem examinations[24,25] on several patients dying of undulant fever in the United States have shown vegetative endocarditis. Brucella organisms have not been demonstrated in the vegetations on the valves in any of these cases. In most instances it may be assumed that the toxemia incident to undulant fever is responsible for the exacerbaton of the endocarditis and that the patient's death is due to cardiac failure rather than endocarditis caused by brucella organisms.

Source of Infection: Our knowledge of the source of infection in undulant fever is still very limited. Carpenter[26] and others have presented considerable presumptive evidence to show that raw milk from infected cows is one of the principal sources of infection. Nearly all of the patients in this series drank raw milk. It is said that Los Angeles County, which has the highest county morbidity for undulant fever in California, uses more raw milk than any county in the United States. There are 700 raw milk producers in this county, the number of cows in each dairy varying from two to ten or more. Eighty per cent of the supply to Los Angeles City is pasteurized, and 65 per cent of the supply outside the city is pasteurized. It is a question whether the facts shown by these statistics may have some bearing on the large number of cases reported from this county. In one dairy of seventy-two cows 38 per cent were positive reactors.

The first test of 4,000 head of cows in certified dairies showed 37.5 per cent of positive reactors. In order to replace the positive reactors, a large number of cows were tested at various purchase points in the United States. Thirty per cent of these cows were positive reactors.

Five thousand and fifty-five blood specimens were received by the University of California Farm for the agglutination test for Bang's disease of cattle during the year ending June 30, 1929. The specimens were from scattered areas throughout the state and from 121 herds of ten animals or more. Sixty-two per cent of the specimens were positive. The general State average of positive reactors is conservatively estimated as 40 per cent to 50 per cent.

Coolidge,[27] Carpenter,[5] and Frei,[23] individually, have given infected milk to several volunteers, but no clinical symptoms of undulant fever were produced. Gabbi[28] and Otero[29] have recently been succesful in infecting individuals by this means.

We are unable to explain the low incidence of undulant fever in children, the principal milk consumers. It has been shown that brucella infection in calves disappears soon after discontinuing feeding infected milk. Perhaps there is a greater natural immunity before puberty, which progres-

sively decreases with the establishment of the sexual function.

There are several goat dairies in California, distributing raw milk. Goat's milk was not a source of infection in any of the patients who contracted their infection in California.

The evidence is fairly conclusive that several patients have contracted their infection by contact with live stock or animal products. We examined the blood of sixty veterinarians and found positive brucella agglutinins in six. In one the titer was 1-40; in two 1-80, in two 1-160, and in one 1-320. Four of the men drank only pasteurized milk. All of these men gave histories suggestive of undulant fever. Several with negative agglutination titers also had had pyrexia of unknown etiology. The incidence of abortus antibodies in the serums of these individuals is much higher than that generally reported for human serums.

In California undulant fever has been recognized as an occupational disease. In most instances there was considerable evidence to show that the brucella infection had been acquired either by accidental inoculation while at work or by contact with infected animals or animal products.

Cornell[21] has suggested the possibility of poorly cooked liver or meat as a source of infection. Other animal glandular products may be included also.

Several attempts[30,31,32,33] have been made to infect humans by injections of live organisms, but all have been unsuccessful. We have sufficient proof in the numerous laboratory infections reported, that inoculation with human abortus strains may take place through abrasions or injections.

Incidence in Animals: We are commencing to learn about the prevalence of this infection among the phyla of the animal kingdom. Emmel and Huddleson[34] have recently described Brucella abortus infection in chickens. Abortus organisms have been isolated from fistulae of horses[35] and it is believed that Brucella abortus is associated rather closely with poll-evil and fistulae. We examined the blood serum of a cat fed infected milk since birth, but found no brucella agglutinins.

Many sources of infection besides those already considered may be revealed by further study. We need more accurate and definite information regarding the source of infection in man. In the mean time, as considerable evidence has accumulated incriminating raw milk as a source of infection, it would seem best that ordinary raw milk be pasteurized before consumption, as a prophylactic measure. Certified milk is safe if regular periodic tests show no positive reactors in the herds.

It is possible to free herds from infection as shows by the records of several of the certified dairy herds in California. In this state certified milk bearing a cap with the seal of the American Association of Medical Milk Commissioners, comes from cows which react negatively to the agglutination test for Brucella abortus.

Traum[36] and Carpenter[37] pointed out that, on rare occasions, brucella organisms may be eliminated in the milk of non-reacting cows. Of three cows which were eliminating brucella

organisms, though their serums were negative, Traum found that one soon became a positive reactor and the other two ceased to eliminate the organisms. He feels that, even though such an animal exists in the herd without detection, the high dilution of the milk from this cow by the rest of the milk from a large dairy, practically frees it from the danger of transmitting infection.

Extreme care should be exercised in the handling of animal fetuses as infection in at least two of the cases reported from California have been traced fairly definitely to this source. Contact with livestock seemed to be a source of infection in a few instances.

NOTE: Dr. Harbinson was taken ill during the Minneapolis meeting. His death took place one week later. (Editor.)

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"Polymorphonuclear Leucopenia" A Proposed Classification

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AGRANULOCYTOSIS was first reported by Schultz in 1922. In the last seven years, many observers have added cases. The number has amounted now to nearly one hundred cases[1]. When one reviews the literature on this disease, he is impressed with its protean manifestations. Blumer[2] has recently drawn attention to the fact that all cases do not conform to Schultz' original description. One finds cases without anginal lesions, with anemia, with only moderate reduction of white cells, etc. The natural inference is, therefore, that agranulocytosis as an entity has not been completely described.

Much has been written in an effort to define the etiological mechanism and symptomatology of this condition. Rose and Houser[3] consider it a non-specific infectious condition. Farley[4] has called attention to the blood picture following arsenical poisoning which follows closely that described for agranulocytic angina. Such cases do not show necessarily any signs of angina. The symptom complex, including high temperature, seems to be a result purely of a chemical intoxication. This is interesting in so far as it excludes any bacterial participation. Farley[4] lays great stress in such cases on the inhibiting effect of arsenic on the bone marrow. I have observed two cases, in which there was a definite agranulocytosis with hectic symptoms following the administration of neoarsephenamine.

Gordon[5] has recently reported four cases under the term "agranulocytosis". He appends a very excellent bibliography. In this article, as in many others on this subject, there is considerable uncertainty and speculation regarding the proper name of this condition. One finds different terms applied—agranulocytic angina, agranulocytosis, malignant neutropenia, etc. The same confusion is found as regards the etiology. There is even some doubt as to whether this condition is a disease entity. The symptomatology is likewise not clearly defined and in the list of therapeutic suggestions one finds much to choose from. There seems at the present only one really constant and universally accepted finding—a polymorphonuclear leucopenia. Even the presence of membranous ulceration is not constant if one accepts all the reports of cases under the term agranulocytosis. There is likewise no distinctive pathological picture of this condition.

Because of this confusing etiological, symptomatological and pathological variability, it is exceedingly desir-

able that there should be some clinical classification, which would be at least a first step in the proper understanding of this disease process and in removing it from its present state of chaos.

Using the one constant finding of the condition as a starting point, the following etiological classification is suggested: 1. Infectious polymorphonuclear leucopenia; 2. Toxic or chemical polymorphonuclear leucopenia; 3. Symptomatic polymorphonuclear leucopenia; 4. Idiopathic polymorphonuclear leucopenia.

In the first group are included those conditions that begin with symptoms of an acute upper respiratory infection, high fever, chills, sore throat, etc., without a history of arsenical medication. Within a variable period, from one to two days, there develops painful swallowing, an ulcerative stomatitis which soon becomes gangrenous, swelling of the neck, malaise, severe toxemia and prostration. Other symptoms are variable. There may develop ulcerations of the vaginal or rectal mucosa, sometimes very extensive and severe. In some patients icterus appears. The liver and spleen may enlarge and there may be a general glandular enlargement. The toxemia increases, delirium supervenes and death usually follows. The course of the disease is usually acute and rapidly fatal, seldom lasting over two weeks, without recovery. Early in the course of the illness, the blood count may be normal. The red cells may or may not be effected. The white cells soon show a decrease and drop very rapidly to complete disappearance if the disease proves fatal. The granular cells are the elements that disappear and there results a relative increase in lymphocytes.

In the second group are included those cases that follow the administration of some chemical, principally the arsenical preparations. Radium poisoning produces practically the same pathological picture. Recently, there have appeared in the literature several articles calling attention to the potential dangers inherent in the administration of arsenical compounds. Most recently Farley[4] reports several of such cases. It is more difficult to outline the onset and development of symptoms in this form of polymorphonuclear leucopenia than that described in the foregoing paragraph. The reason is that the individual susceptibility to arsenic varies so much. Some patients show a marked dermatitis, high temperature, malaise with a polymorphonuclear leucopenia of varying degrees, etc., following a single injection of arsenic. Other patients will manifest symptoms only after a large series of such injections. Likewise, in some there are ulcerative or gangrenous lesions present, while in others such signs never appear. It would seem that the presence or absence of these membranous ulcerations depends on the rate and degree of the disappearance of granulocytes from the blood stream.

In the infectious type it is not clear whether the ulcerative lesions precede or follow the reduction of white cells. There are numerous cases reported of this form in the early stages of which the white cells are normal. At the same time, there are what seem to be unquestionable cases of the toxic form

that begin with severe ulcerative lesions in the mouth or throat. The exact relationship, therefore, between the time of ulceration and decrease in the polymorphonuclear leucocytes is not always clear. One finds in the literature a diversity of thought regarding this phenomenon. It has been suggested by some that the ulcerations are dependent upon the disappearance of the polymorphonuclear leucocytes, while others are inclined to consider the polymorphonuclear leucopenia the result of the membranous ulcerations. It is conceivable that there might be a qualitative change in the granulocytes that could account for the loss of local resistance and subsequent ulcerations before a quantitative change in them is demonstrable.

In the toxic or chemical group, dryness in the pharynx, which is often the first symptom, followed by intense congestion and frequently extravasation of blood into the tissues with necrosis or sloughing in which very little odor is noticeable, characterizes the progressive changes. The cervical glands usually become swollen, thus giving the characteristic swelling of the neck. All of these symptoms may or may not be associated with skin manifestations. From my own observations I am inclined to believe that frank ulcerations or gangrenous lesions do not occur without a material diminution of the polymorphonuclear leucocytes.

The clinical picture, therefore, of a rather severe malaise and prostration, fairly high temperature (102 to 105 degrees) with or without gastrointestinal upset, often associated with a diffuse erythematous dermatitis, frequently involving the mucous membrane, with or without frank ulcerations, coming after or in the course of arsenical medication principally, and accompanied by a gradual decreasing white cell count—polymorphonuclear leucopenia—should be considered until proved otherwise that of a toxic or chemical polymorphonuclear leucopenia.

The mortality in this type does not seem to be as high as in the infectious form. The variable would appear to be the susceptibility of the hemopoietic system and its recuperative power.

The group, symptomatic polymorphonuclear leucopenia, would include those conditions in which such a blood picture is found and is of such a degree as to be considered a determinant in the course or prognosis of the primary disease. Such a classification is not designed to change the name of the primary process but to avoid confusion in terminology and diagnosis. For example, one finds in the more severe pernicious anemias a polymorphonuclear leucopenia, which is a symptomatic manifestation, but differential diagnosis can be made. Likewise, in some of the leukemias, notably the so called aleukemic leukemia, which is diagnosable by careful blood studies, one may find definite polymorphonuclear leucopenia. The same may be said of the secondary or aplastic anemias, such as occur in benzol poisoning and the severe streptococcic blood stream infections. The recognition of the granulocytic picture in such conditions as a symptomatic process would help a great deal in avoiding diagnostic confusion.

Finally, in the group, idiopathic polymorphonuclear leucopenia, would be included those cases the etiology and nature of which are so obscure as to prevent their inclusion in one of the other three groups.

As stated in the beginning, the classification that has been suggested is intended purely as a clinical one. There is no constant bacteriological, symptomalogical or pathological picture of "agranulocytosis" or polymorphonuclear leucopenia. By combining the mode of onset and etiological information, one can, by the classification offered herein, at least acquire a convenient working differentiation of this very interesting disease process. By using such a classification, the morbidity statistics of this condition may begin to mean something. As it is, they are just a heterogenous mixture of pathological states manifesting a polymorphonuclear leucopenia.

Summary

A clinical classification of the states exhibiting a polymorphonuclear leucopenia has been outlined. The classification is based on the mode of onset and the etiology and is: 1. Infectious polymorphonuclear leucopenia; 2. Toxic or chemical polymorphonuclear leucopenia; 3. Symptomatic polymorphonuclear leucopenia; and 4. Idiopathic polymorphonuclear leucopenia.

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Proctosigmoidoscopy: A Medical Diagnostic Procedure*

A Plea for a Wider and More Frequent Use of This Method by the Internist.

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THE proctosigmoidoscope brought into being the surgical specialty of proctology much the same as the stomach tube gave birth to gastroenterology and the electrocardiograph to cardiology. As a result, sigmoidoscopy became a surgical procedure, an instrument to be used mainly by proctologists and general surgeons. The method, in its earlier days was, and in many places still is, attended by preparation which rivals that of a major surgical procedure. Indeed, even at this late day it is not uncommon to note the posting of proctoscopic examinations upon the operating room schedules of many of our large hospitals. This state of affairs has passed from one medical generation to another and as a result few internists employ proctosigmoidoscopy as a diagnostic procedure. It is felt that this is a mistake, that proctosigmoidoscopy is an essential medical diagnostic procedure to be used by internists because of the very nature of the conditions in which its employment is indicated. It is to call attention to these facts that this paper is written. Diagnosis, in the main, is a medical problem. If it only were possible to offer this very general and obvious fact as a reason for the use of proctosigmoidoscopy by the internist, it would appear that this alone would be sufficient to place the procedure in the same category as that of other endoscopic methods in general usage such as opthalmoscopy, laryngoscopy, sinus transillumination, otoscopy and the like.

Concretely, however, the reasons for the necessity of the employment of the proctosigmoidoscope by the internist as a diagnostic method, are more cogent. It is felt that an examination is incomplete without submitting the patient to proctosigmoidoscopy when there is a history suggesting even the slightest deviation from the usual bowel habits. Besides, usually cases are seen first by the internist, and if there be any virtue in the establishment of early diagnoses, then many opportunities for so doing are lost if one waits until manifestations become more pronounced or until the patient

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reaches the proctologist or surgeon at a later date. Also, many of the problems encountered within the intestine are primarily medical in nature. Take the question of the colitides! These conditions are medical essentially; they become surgical secondarily: upon the failure of proper medical management after a reasonable trial, or upon the arising of complications which call for surgical intervention, or upon manifestations which are growing worse that cannot be controlled by medical means. Obviously, the use of the proctosigmoidoscope by the internist is essential here. To attempt to study, diagnose and manage these problems without proctosigmoidoscopy would appear in the same light as investigating and treating a complaint of sore throat without ever having inspected the mouth and pharynx. Also, the topical application of medicaments in localized conditions within the rectum or sigmoid through the sigmoidoscope is, in our opinion, not outside of the province of the internist. Even in cases of "Irritable Colon", the functionally disordered bowel, proctosigmoidoscopy by the internist is indicated, for the problem is purely medical in nature. Further, those conditions recognized as surgical from the standpoint of treatment—hemorrhoids, polypi, malignancy, fistulae, etc.,—are of as much concern to internists as to proctologists and surgeons, for these cases usually are seen first by internists, and since early and correct diagnosis here is essential too, proctosigmoidoscopy should be employed by the physician to accomplish this satisfactorily.

The importance of proctosigmoidoscopy by the internist will be appreciated further, when it is realized that most of the intestinal involvements, functional and organic, evidence their earliest manifestations in the rectum and lower sigmoid and consequently are within reach of the instrument; and also that the roentgen-ray as a method of diagnosis in colonic disorders, is least satisfactory in rectal and lower sigmoidal conditions.

In recent years, the proctosigmoidoscope has assumed other usages which are purely medical in nature. The securing of material for bacteriological study directly from the suspected or involved rectum or sigmoid through a proctosigmoidoscope has been found superior to that obtained from defecated feces, for when the material is obtained through the instrument it is fresh and is procured directly from the site desired. Methods have been devised and elsewhere described of securing material for bacteriological examinations directly from the rectum or sigmoid from the exact point desired through a sigmoidoscope without contamination from surrounding sources or by the instrument[1]. Incidentally, this procedure was originally employed in our bacteriological studies with regard to etiology in chronic ulcerative colitis[2]. In addition, it has been demonstrated that diagnosis of human intestinal protozoa can be improved about 350% by studying dejecta secured directly from the sigmoid through a sigmoidoscope than by an examination of defecated feces[3]. These are medical problems pure and simple in which the use of the proctosigmoidoscope by the internist is a pre-

requisite to the proper application of these newer methods.

At Johns Hopkins, proctosigmoidoscopy has been practiced for some years as a medical diagnostic procedure: on the medical wards and in the Gastro-Intestinal Clinic members of the staff employ this method when indications arise. The instrument is inserted from 20 to 30 cms., without the aid of any type of anesthesia, narcotic or sedative, and the glamor as well as the elaborateness still attending this method of diagnosis in some places, has been removed.

Students are being given the medical point of view regarding proctosigmoidoscopy and intestinal disorders. To this end, life-like and life-sized models of conditions in the rectum and sigmoid as seen through a proctosigmoidoscope have been devised for individual and group instruction thus enabling either the presentation of the entire gamut of lower bowel disorders almost simultaneously, or the demonstration of a particular condition in the absence of a suitable case[4].

In view of the aforegoing, it is urged that proctosigmoidoscopy be regarded as a medical diagnostic procedure, that it assume a position in the hands of the internist similar to that of such methods as opthalmoscopy, otoscopy, laryngoscopy, sinus transillumination and the like, and that students be taught this point of view.

SUMMARY

Proctosigmoidoscopy has been urged as a medical diagnostic procedure, a method to be used by internists like opthalmoscopy, to facilitate the problem of early diagnosis in intestinal manifestations; and also because the very conditions in which proctosigmoidoscopy is employed, are, in many instances, medical problems essentially, or are, in other instances, at least of as great importance to physicians as to surgeons and proctologists.

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Editorial

HEPATIC LESIONS ASSOCIATED WITH EXOPHTHALMIC GOITER

For a number of years we have noted that the livers of patients dying with exophthalmic goiter in the University Hospital presented significant pathologic changes. Many showed some degree of simple or pigment atrophy, but the most common and striking hepatic change was the very frequent occurrence of a marked diffuse fatty degenerative infiltration, bearing all the earmarks of a severe toxic process. In a number of cases this lesion has been so marked as to call forth comparisons with the classical phosphorus liver. To make the resemblance to the latter condition more close, the hearts and kidneys of the same patients presented a marked fatty degenerative infiltration. In one patient, a young girl of seventeen, who died of fulminating exophthalmic goiter symptoms of only twenty-four hours duration, these pathologic lesions were so marked as actually to cause a suspicion of phosphorus poisoning. In cases of exophthalmic goiter in which death occurred after operation and anesthesia, it is impossible to attach direct importance to the presence of an acute fatty degenerative infiltration of heart, liver, and kidneys, inasmuch as this parenchymatous change is of frequent occurrence after prolonged anesthesia. But since we have found similar severe grades of diffuse fatty infiltration in the liver, myocardium, and kidneys of patients dying with fulminating Graves' symptoms, who had not been subjected to anesthesia and operation, the writer has come to look upon the condition as an essential part of the pathology of severe Graves' attacks, and has explained them in his own mind as the result of acute disturbances in the oxygenation of the body, resulting from or dependent upon the Graves' syndrome. If this be true the fatty degenerative infiltration would be a secondary pathologic lesion of Graves' disease and not a primary one. We have, however, noted from time to time that the livers of Graves' patients show a peculiar form of chronic parenchymatous hepatitis in the form of lymphocyte infiltration, bile duct proliferation, and increase in stroma of the islands of Glisson. These changes may be present in but slight degree, or they may be so marked as to lead to the diagnosis, both upon the gross and the microscopic examination, of an atrophic cirrhosis. From the latter condition, however, this picture differs in that the inflammatory changes are more irregularly distributed in the liver, and also in respect to the more or less well-marked intralobular distribution at the periphery of the lobules, which is present in the more advanced cases. In order to determine the significance of these hepatic changes in

Graves' disease, Weller* undertook a controlled study of a group of such cases. Forty-four autopsies upon patients showing graves' disease, clinically and pathologically, were selected, taking care to exclude any case which had cholelithiasis, cholecystitis, syphilis or any other associated condition which might produce periportal changes similar to those under investigation. Of this group 6 cases showed no hepatitis, 16 cases showed a slight or moderate hepatitis, while 22 cases showed a well-marked chronic hepatitis of the type described above. A control series of autopsies was then set up, matching each patient with another of the same sex and of approximately the same age, excluding the same group of conditions known to produce pathologic changes in the liver as before, but excluding Graves' disease. In this second series, made to be as nearly equivalent to the first as possible, except that all evidence of a Graves' constitution or syndrome was lacking, 30 cases showed no hepatitis at all, 13 cases a slight or moderate hepatitis, and in only 1 case a well-marked hepatitis. It is significant that this one case was from a patient with a pituitary tumor and well-marked hypoplasia of the adrenals. Such a marked difference in the incidence of hepatitis in the two groups seems to establish the fact that a definite significance attaches to the coincidence of Graves' disease and hepatitis. Whether a direct or indirect relationship exists between them can at present be answered only upon very uncertain hypothetical grounds. Weller summarizes his findings, as follows: "A well-marked chronic parenchymatous hepatitis was found at autopsy in 22 of 44 selected cases of Graves' disease, while but 1 case of the same degree of hepatic lesion was found in a control series of the same number of autopsies. In the Graves' disease group only 6 showed no evidence of hepatitis, while in the control series 30 out of the total of 44 cases showed no hepatitis. The coincidence of hepatitis with exophthalmic goiter is therefore significant and is in accord with clinical observations of the occurrence of functional disturbance of the liver in cases of Graves' disease." Jaundice has been frequently observed in patients suffering with Graves' disease. Under such titles as "Jaundice Occurring in Persons Suffering from Exophthalmic Goiter," "Acute Yellow Atrophy Associated with Hyperthyroidism," and "Basedow's Disease with Subacute Yellow Atrophy," there have been reported occasional examples of very severe degenerative hepatitis in patients with hyperthyroidism. Less marked degrees of jaundice have likewise been frequently noted, so that it is now well known that many patients with thyrotoxicosis show a yellowish tint of the sclerotics and some a decided icterus. The latter event is thought to have a grave prognostic significance. Studies of impaired liver function in Graves' disease have been carried out by only a few observers. Youmans and Warfield found that 50 per cent of a series of 44 patients with thyrotoxicosis showed an impairment of liver function according to the methods of testing used by them. Loss of weight

*Presented before the Association of American Physicians, 1930.

was the only feature of the disease which seemed to bear a definite relation to the impairment of liver function. Simonds and Brandes rendered dogs thyrotoxic by heavy thyroid feeding for periods varying from 32 to 100 days. They found that in such animals the liver did not lose weight proportionately with the rest of the body, while with starvation the liver lost weight in greater proportion than the body as a whole. Since the livers of the thyrotoxic animals were practically devoid of glycogen something must occur to counterbalance the loss of glycogen. It was suggested that increased functional activity and increased rate of blood flow might explain the failure of the liver to lose weight proportionately to the body as a whole. There are numerous observations reported in the literature concerning the carbohydrate metabolism in thyrotoxicosis. Cramer was the first to show that the feeding of active thyroid material to rabbits, cats, and rats, led to a lowering or disappearance of the liver glycogen in spite of an abundant carbohydrate food supply. Numerous observers have confirmed this finding. Abeling, Goldener, and Kobori showed that the livers of animals fed with thyroxin no longer formed glycogen. If to the diet of these animals during the thyroid feeding, abundant fat was given, the livers again showed glycogen deposits. Ascher and Galvo-Criacho found that in animals made absolutely free of carbohydrate by thyroid-feeding and phloridzin, the addition of fat to the food increased the output of sugar. From this, these authors decided that the hyperthyreotic liver possessed the ability to form glycogen, but could not fix it, so that after its formation gave it up. The effect of thyroid material upon the carbohydrate state of the organism is so striking that the latter may be made wholly carbohydrate free through the feeding of thyroid material and the use of phloridzin. Not only the liver, but also the muscles are hereby rendered practically glycogen-free. It would appear that not only is the consumption of glycogen increased, but also its new formation and storage. Stimulated by the results of animal experimentation, Kugelmann (Klin. Wschr., August 16,1930) studied the carbohydrate metabolism of human cases of Basedow's disease. It has been known for a long time that there is an alimentary glycosuria in Graves' disease; this was first described by Kraus and Ludwig. The administration of 100 g. of grape-sugar is sufficient to cause a well-marked glycosuria, and the blood-sugar increases and remains at a higher point than is the case in normal individuals. This change in the blood-sugar curve occurs, however, so frequently in so many other diseases that its significance is thereby limited. According to the studies of Bang and Traugott, it would appear probable that this form of "diabetic" blood-sugar curve is found only when the glycogenic function of the liver is damaged. Further investigations of the carbohydrate metabolism of the Basedow cases along the line of the study of the ketone-bodies shows that in thyrotoxic individuals who are given a carbohydrate-free diet for two days, there is such a significant increase of ketone-bodies in the blood as was formerly thought to occur only in sub-

comatose diabetics. In the normal individual the fasting value of ketone-bodies never exceeds 3.5 mg. per cent of acetone-acetic acid and 5.5 mg. per cent of B-oxybutyric acid. In the thyrotoxic patient the fasting value of ketone-bodies rises to 16 mg. per cent of acetone-acetic acid and 18 mg. per cent of B-oxybutyric acid. This method of investigation would prove that the Graves' patient has a lowered glycogen-reserve available for metabolism. This changed state of the glycogen-depots can be demonstrated also by the study of the blood-sugar curve after intravenous injections of insulin. If we inject 10 units of Wellcome's insulin intravenously into a normal man, there occurs regularly in the first ten minutes after the injection an increase in blood-sugar of 15—20 mg. per cent; then a typical fall. Bűrger demonstrated that this primary increase of blood-sugar is dependent upon the glycogenic function of the liver. In the cases of Graves' disease studied by Bűrger's method by Kugelmann, none showed this initial hyperglycemia. This is further proof of the poverty in glycogen in the hyperthyreotic liver of Graves' disease. The study of the blood- and urine-sugar after the oral administration of levulose throws further light upon the processes of the intermediary carbohydrate metabolism. Strauss first introduced alimentary levulosuria as a method for testing the liver function. Isaac and Adler showed experimentally that of all the organs and cells of warm-blooded animals only the liver is capable of transforming levulose into dextrose. According to Isaac the alimentary levulosuria is dependent on the fact that the part of the levulose which is not converted into glycogen or is burned, in case of functional inability of the liver to convert levulose into dextrose, passes as levulose into the blood and is excreted in the urine. Later investigations of Isaac showed that the occurrence of levulosuria is not sufficient to make a positive diagnosis of disturbed liver function. Numerous investigators have shown that the frequently occurring alimentary levulosuria of pregnant women is in most cases a pure renal levulosuria and does not in any way point to a functional disturbance of the liver. Isaac therefore recommended that after the administration of 100 g. levulose the blood sugar be determined at varying periods during several hours following its administration. By this method he found that normal individuals showed either no or a very slight rise in blood sugar, but never exceeding values over 120 mg. per cent. On the other hand in individuals with hepatic disease he found a decided hyperglycemia which persisted for some hours. This has been confirmed by Spence and Brett, Bornstein and Holm, Hetényi, Grafe, and others. Isaac differentiated the various sugars during this hyperglycemia and found that the height of the blood-sugar after administering of levulose depended in some cases upon an increase in the concentration of dextrose, and in other cases upon an increase in the levulose content of the blood. He decided from this that the hyperglycemia, after the administration of levulose, indicates surely a functional disturbance of the liver. This has been confirmed by Bodansky who after chloroform and phosphorus poisoning found that the

administration of levulose caused a hyperglycemia. This problem had previously not been attacked from the standpoint of Graves' disease. Falta had reported in a few cases of Graves' disease the occurrence of an alimentary levulosuria. As already shown above this finding is not sufficient evidence of disturbed hepatic function. Abelin and Miyazaki have shown in animal experiments that the administration of levulose in healthy animals produced no essential change in the respiratory quotient; but that the same amount of levulose after thyroid feeding produced a marked increase in the respiratory quotient, even to values of 1.0. They explain this on the ground that levulose, which under normal conditions is only in a small degree oxidized, is, after thyroid feeding, made use of to furnish energy and is fully burned. Kugelman carried out his studies along the lines indicated by Isaac and Grafe. The blood-sugar estimates were made in the morning, the patient fasting, according to the method of Hagedorn-Jensen. After the administration of 100 g. levulose, the blood-sugar was taken again at ¼ and ½ hours. In normal individuals the blood-sugar increased but slightly during the first half hour. Values over 120 mg. per cent were never found. At the latest the fasting value had returned after two hours. In patients with Graves' disease, the blood-sugar curve was found to be much higher, reaching regularly values of 160-180 mg. per cent. Even after three hours the curve had not fallen to its original value. The Graves' patients show the same blood-sugar curve as that described by Isaac and Grafe for patients with hepatic disease. From this Kugelmann concludes that we can now say with certainty that the thyrotoxic liver suffers not only severe injury in its glycogen depots, but has also lost the capacity to change large amounts of levulose into dextrose and to utilize the latter. For the first time it has been shown that in Graves' disease there is a functional disturbance of the liver which expresses itself in a pathologic condition of the intermediary carbohydrate metabolism. Just what relationship these functional changes bear to the histologic lesions of the liver in Graves' disease remains to be shown. There is a strong possibility that there is a direct relationship between them. The hepatic lesions are probably directly related to the altered metabolic changes associated with thyrotoxicosis. A high basal metabolism has become an almost over-rated symptom of Graves'. The investigation of the gaseous interchange and the information it gives us as to metabolism is only a small part of the whole metabolic process, but throws no light upon the essential changes in the intermediary metabolism. These evidences, both pathologic and functional, of the disturbed glycogenic function of the liver, are, therefore, of prime importance, and further studies along these lines may throw important light upon what lies behind the thyroid in the pathogenesis of the Graves' syndrome.

Abstracts

Changes in the Blood Chemistry in Malignant Disease with Special Reference to Carbohydrate Tolerance and Alkalosis. By PAULINE BEREGOFF (The Jour. of Cancer Research, October, 190).

The purpose of this investigation was to observe the alterations in the blood chemistry associated with malignant disease, and to determine the value of such changes in the diagnosis of human cancer. Freund (1885) and Trinkler (1890) found in cancer patients a low tolerance for sugar and claimed that the carbohydrate tolerance test was of diagnostic value in cancer. Rohdenburg, Bernard, and Krehbiel (1919) studied the sugar tolerance in cancer patients and found a low tolerance for sugar in all cancer patients examined, but as their series was small, they did not base any contentions on their findings. In the same year Edwards reported several cases of carcinoma in which the glucose tolerance test was low. He considered this test of greater value as a method of eliminating the presence of cancer than of establishing its existence. The failure to establish a specific glucose tolerance curve, as is found in cancer, he considered strong evidence against the presence of malignant disease. In 1927, Reding and Slosse showed that cancer patients possess a lower tolerance to glucose. In 1928, Reding attempted to demonstrate alterations in the blood chemistry of patients suffering from cancer or having a predisposition to cancer. In each case he determined the pH, the total CO_2 (free and combined) and the concentration of the ionized calcium. Alkalinity, fall of CO_2, and fall in the concentration of ionized calcium, he found to be constant phenomena associated with cancer. In 1929 these findings were confirmed by Reding and Slosse. In the same year Schreus also reported that the blood chemistry of carcinoma patients showed a moderate alkalosis. Cori and Cori have pointed out that abnormally large amounts of glycogen are present in malignant tumors. Warburg showed that there is a distinct difference in glycolysis of the cancer cell as compared with glycolysis in normal tissues. The glycogen metabolism of cancer is about 8 times that of working muscle and about 100 times that of resting muscle. According to Warburg and Cori and Cori the excessive amount of lactic acid produced by cancer cells points to abnormal carbohydrate metabolism in the cancer cell itself, whereas the observations indicate an abnormal carbohydrate metabolism in the organism as a whole. Jackson claims that the character of the sugar curve may serve as an indicator of the response that may be expected to radiation and surgery. Beregoff studied a series of 300 patients in whom the blood showed a tendency towards alkalosis, low carbohydrate tolerance, deficiency in calcium, and a low carbon dioxide content. All bloods of cancer patients examined in this investigation exhibited a positive carbohydrate curve and a tendency towards alkalosis. However, positive carbohydrate curves were obtained in other pathologic states, such as hyperthyroidism, acromegaly, and diabetes, but in these conditions no alkalosis was demonstrable. As an indication of the presence of malignant disease a positive carbohydrate curve is significant only in the presence of alkalosis. Examinations of the blood of 25 individuals not suffering from cancer, and without family history of cancer, yielded a negative carbohydrate curve in every instance and the pH of the bloods was within normal limits. The concentration of the ionized calcium averaged 22.6 mgm. per liter. It would appear from these experiments that the carbohydrate tolerance test and the hydrogen ion concentration are of greater value in eliminating the presence of malignant disease than of proving its existence.

The Clinical Value of Tests of Liver Function. By GEORGE MORRIS PIERSOL (Canad. Med. Assoc. Jour., October, 1930, p. 524).

Piersol sums up his discussion of hepatic functional tests as follows: From his experience with liver function tests, as applied to a considerable group of patients suffering from various disorders, the three most practical and useful tests clinically are ((1) the retention of the dye bromsulphthalein; (2) the estimation of the serum bilirubin, particularly, the determination of the icterus index; and (3) the occurrence of urobilinogen in the urine. The retention of bromsulphthalein is not an early indication of liver dysfunction. The degree of retention is a helpful indication of the extent of liver damage. When dye retention occurs other functional tests are also positive, but we have not found any noteworthy degree of bromsulphthalein retention when the ordinary clinical evidences of liver disease were not present. The estimation of the serum bilirubin is a most useful test of liver function, since it frequently indicates the presence of a latent icterus before liver disorders can be recognized by clinical signs, and the persistence of bilirubin in the blood after all other evidences of liver disease have disappeared. He regards an increase in the urobilinogen as the most delicate test of impaired function. Urobilinogen is increased even when damage to the liver parenchyma is exceedingly slight. It is persistently increased as long as any residual hepatitis remains, and it is the one test which has been positive in a certain number of cases in which liver disease was suspected, but could not be proved clinically. Because of the liver's multiple functions and because of its extraordinary capacity and remarkable ability to regenerate, it must be admitted that from the standpoint of the clinician who is seeking some means whereby impaired liver function can be recognized, before gross clinical evidences of liver disturbance occur, the tests for liver function that are available at present have hardly justified our earlier expectations. This is the more true because in all focal lesions of the liver, especially those without biliary obstruction, functional tests yield no useful information. They are, however, of some help in differentiating the various types of jaundice and in the diffuse disturbances of the liver, in which by means of them, we are enabled to estimate with some degree of accuracy, the extent and duration of the liver damage, so that they are undoubtedly of prognostic value.

Uroselectan as a New Renal Functional Test. By W. TOURNÉ and E. DAMM (Klin. Wschr., August 23, 1930).

The uroselectan blood-curve falls steeply in the first two hours, less steeply later. When the renal function is normal no more uroselectan is present in the blood after 4 hours. Values under 0.5 g. after 4 hours indicate a low grade of renal insufficiency. Values over 0.5 g. indicate a higher grade of renal damage. According to the degree of renal insufficiency more or less large amounts of uroselectan are found in the blood. The use of the 4 hour uroselectan test in the blood is recommended as a new test for urinary retention.

The Treatment of Cardiac and Aortic Syphilis. By A. MEYER (Münch. Med. Wschr., 1930).

The treatment of syphilitic myocarditis and aortitis by means of salvarsan is, according to Meyer, not always devoid of harm, and may lead to unpleasant consequences through the development of the Herxheimer reaction. He advises that patients having aortic and cardiac syphilis be given a milder form of antisyphilitic treatment in the form of a ""Schmierkur", or intramuscular injections of bismuth, or by internal medication with iodide. When salvarsan is used it should not exceed 5-6 g. for the total amount employed. The treatment should be intermittent and extended over prolonged periods. R. Fischer (Wien. Klin. Wschr., 1930) believes that the suspicion of aortic syphilis, even in the presence of a negative Wassermann, is sufficient to justify active treatment. An electrocardiogram is necessary to show the condition of the coronary arteries. If this shows coronary disease, antisyphilitic treatment is absolutely contra-indicated. Neosalvarsan is the best remedy for the treatment of aortic syphilis. Fischer gives it at weekly intervals in doses of 0.075, 0.1, 0.15, and 0.3 gm. When aortic insufficiency is present, with slight changes in the electrocardiogram of

the left ventricle, after the dose has reached 0.3 g., this should be repeated only monthly, in order to give the heart time to compensate, by the development of the collateral circulation, for the cicaricial narrowing of the coronary arteries.

Investigations as to the Place of the Liver in the Intermediary Metabolism. By KARL PASCHKIS (Klin. Wschr., October 11, 1930).

The rôle played by the liver in protein metabolism remains still an unsolved problem. The protein material of the food is either wholly or for the greater part broken down in the intestine to the simple fundamentals, the amino-acids, and carried in this form through the portal vein to the liver. It is a question whether desaminization of the amino-acids is one of the functions of the liver, or whether this process occurs in the peripheral tissues. Van Slyke, Folin, and Denis hold different views on this matter. Mann and Magath have proved experimentally than the dog deprived of his liver cannot desaminize the amino-acids. Clinically, the important question is whether in individuals with hepatic disease any disturbance of protein metabolism takes place. In acute yellow atrophy, as well as in many cases of simple jaundice, leucin and tyrosin appear in the urine, but this may be the result of the associated organ autolysis and not the result of a lowered power of desaminization on the part of the liver. Glässner some years ago found that the administration of amino-acids to patients with liver disease led to an increased output in the urine. Other invesigators have had for the greater part negative results. All of these experiments which are based upon the intravenous administration of amino-acids are worthless, because of their wholly unphysiologic character. Paschkis has systematically administered amino-acids perorally to patients with liver disease, particularly to those showing a simple icterus following the administration of neosalvarsan for treatment of secondary lues. Most of these experiments were made with glykokoll, others with leucin, alanin, and asparaginic acid. The amino-acid content of the blood was taken before the experiment, and at intervals of 1, 2, 3, 4, and 5 hours afterwards, by the colorimetric method of Folin. Normal controls show after the oral administration of 50 g. glykokoll an increase of the amino-N in venous blood. This increase is much higher in most cases of simple icterus. When the procedure was repeated after the disappearance of the icterus the increase is much less. For example, one patient with simple icterus at the height of the affection, showed after the administration of 50 g. glykokoll an increase of the blood amino-N of over 22 per cent over the fasting content. After the disappearance of the jaundice the same experiment produced a rise of only 33 per cent. No marked parallelism with disturbance of other functions of the liver was shown either with carbohydrate assimilation or with the elimination of bile-pigment. The pathologic amino-acid curve persisted after the icterus. In liver cirrhosis, the height of the rise can be affected by the lessened absorption due to the portal stasis. The amino-N value of the peripheral venous blood is dependent naturally not only on the liver function, but in these investigations the renal component and the renal threshold for amino-acids may be ignored, since in the cases studied there were no complications on the part of the kidneys. On the other hand the absorption capacity of the peripheral tissues plays a rôle. Since, however, the extreme curves were found only in patients with liver disease, and after the disappearance of the liver affection the alimentary amino-acidemia was again slight, the curves obtained may be taken as demonstrating a functional disturbance of the liver.

Clinical and Therapeutic Experiences in 650 Cases of Pneumonia. By C. E. SCHUNTERMANN (Med. Klin., 1930).

Croupous pneumonia due to pneumo-cocci is a disease of middle life, 20-40 years. The relation of males to females affected is about 4:2. The mortality for the individual ages varied from 8.6 to 15.3 per cent in a curve from 18 to 40 years. More cases occurred in the first four months of the year than in the later ones. The lower lobes were most frequently involved, the right more often than the left. The prognosis was determined by biologic factors. Double-sided pneumonias or cases with involvement of the upper lobes

showed a greater mortality. The most important factor in the treatment was complete psychical and bodily rest. Further, the treatment consisted in combating the toxic component and in assisting the heart and vasomotor shystem. The use of quinine lowered the mortality. Quinine-urethane and solvochin were employed. The use of quinine should be begun as early as possible. By doing so postpneumonic complications may be avoided.

Syphilis of the Stomach as Seen Roentgenologically. By J. G. SCHLIFFER (Arch. Verdauungs Krankh., 1930).

The anatomical changes produced by syphilitic affections of the stomach may be visualized by x-ray examination. The differential diagnosis is difficult, however, because of the similarity of the syphilitic affections to those of other organic diseases of the stomach. Gummatous infiltration and hyperplasia and the syphiloma have their seat in the submucosa in the great majority of cases. In gummatous hyperplasia one sees a circular narrowing of the affected part. The contours are sharply delineated. The central canal lies centrally and runs straight. Peristalsis is diminished or absent. The barium meal passes the narrowed portion without hindrance and quickly. Under specific treatment these changes lessen or wholly disappear. Contraction processes when predominating tend to progress. Roentgenologically, the stenosed portion becomes narrower, the contours sacculated, the central canal is displaced somewhat, and the passage of material often markedly hindered. In the reversible form three types may be distinguished: 1, the prepyloric type (canteen stomach); 2, the median type (hour glass stomach); and 3, the total type (microgastria). In the irreversible form there are also three types: 1, pylorus stenosis; 2, cicatricial hour-glass stomach; 3, syphilitic total contraction of the stomach (microgastria). Gummas and gummatous ulcers are distinguished roentgenologically by the atypical character of the picture. Of significance is the determination of the presence of marked anatomical changes wholly out of proportion to or even contradictory to the clinical picture.

Reviews

Physiological Chemistry. A Textbook and Manual for Students. By ALBERT P. MATHEWS, Ph.D., Carnegie Professor of Biochemistry, University of Cincinnati. Fifth Edition. 1223 pages, 107 figures. William Wood and Company, New York, 1930. Price in cloth, $7.00.

This new edition has much new matter added, particularly in the chapters on the vitamins, the internal secretions, the carbohydrates, the porphyrins, the bile pigments and the bile salts. The progress that has been made in our knowledge of the enzymes has also been added. The important isoprene, or polydrene, syntheses are brought in for the first time. The only revision of nomenclature has been the change of the term lipin to lipid. Part I treats of the chemistry of protoplasm and the living cell under the following heads: Chapter I, The General Properties of Living Matter; Chapter II. The Glucides or Carbohydrates; Chapter III, The Lipids. Fats. Oils. Waxes. Phosphatides. Sterols; Chapter IV, the Proteins; V, the Physical Chemistry of Protoplasm. Part II treats of the mammaliam body considered as a machine, its growth, maintenance, energy transformations, and waste substances, under the following heads: Chapter VI, Animal Heat; Chapter VII, The Raw Materials or Foods; Chapter VIII, Salivary Digestion; Chapter IX, Digestion in the Stomach; Chapter X, Digestion in the Intestine; Chapter XI, Absorption; Chapter XII. The Circulating Tissue. The Blood; Chapter XIII, The Master Tissue of the Body. The Brain; Chapter XIV, The Contractile Tissues. Muscle; Chapter XV, The Connective or Supporting Tissues. The Bones. Cartilage. Teeth. Connective Tissue; Chapter XVI, The Cryptorrhetic Tissues. The Thyroid. Parathyroid. Hypophysis. Suprarenal. Reproductive Glands. Pineal Gland. Thymus; Chapter XVII, The Skin and Eye; Chapter XVIII, The Excretions of the Body. Urine; Chapter XIX, The Metabolism of the Body Considered as a Whole. Carbohydrate Metabolism; Chapter XX, Protein Metabolism of Body; Chapter XXI, Metabolism Under Various Conditions. Vitamins; Chapter XXII, Respiration; and Chapter XXIII, Chemical Defense Against Disease. Part III is concerned with practical work and laboratory methods. Each chapter is followed by a list of papers bearing on the subject treated in that chapter. The material of the book appears to be full and brought up-to-date. The author has expressed himself in a clear and concise style. The book is readable and understandable. Five editions since 1915, and an Italian and Spanish translation speak for a successful reception. The 337 experiments outlined under practical work cover thoroughly the field of laboratory work in biochemistry. The directions given for each experiment are sufficient and to the point. Superfluous and extraneous matter is omitted. This book can be recommended without reserve to the student in physiological chemistry; and to the physician who wishes to refresh and to add to his knowledge of the subject.

Handbook of Pediatric Procedures. By FRANCIS SCOTT SMYTH, M.A., M.D., Associate Professor of Pediatrics. University of California; Pediatrician-in-Chief, University of California Hospital and Out-Patient Department; and Edith I. M. Irvine-Jones, M.B., Ch.B., Instructor in Pediatrics, Washington University School of Medicine, Assistant Physician, St. Louis Children's Hospital. 212 pages. The MacMillan Company, New York, 1930. Price in cloth, $2.50.

The publication of this book has been prompted by the apparent demand for brief

descriptions of methods for the study and treatment of disease in children. The outline form and didactic presentation of the material have been adopted for the sake of brevity and ease in reference. The treatment of the material falls into Section A—Diagnosis, three chapters being devoted to History, Physical Examination, and Laboratory Diagnosis; Section B—Therapy, containing seven chapters treating successively of Dietetic Therapy, Biologic Therapy. and Prophylaxis; Physical Therapy; Drug Therapy; Fluid Introduction in Sick Children; Emergency Treatments and Some Common Principles. This book is in reality a small and much condensed manual of pediatrics, and has all of the defects of such abbreviations. Such may have a certain value as a convenient pocket aid to memory for internes in pediatrics; but if, as the preface would indicate, there is a demand for brief outlines of this type among practitioners, one is led to believe that a superficial machine type of knowledge is a desideratum.

Intestinal Tuberculosis. Its importance, Diagnosis, and Treatment. A study of the Secondary Ulcerative Type. By LAWRASON BROWN, M.D., Consultant to the Trudeau Sanatorium, Saranac Lake, New York; and Homer L. Sampson, Roentgenographer of the Trudeau Sanatorium, Saranac Lake, New York. Second edition, Thoroughly Revised. 376 pages, 122 engravings, and 2 colored plates. Lea and Febiger, Philadelphia, 1930. Price in cloth, $4.75 net.

This second edition has been fully revised and enlarged. The methods of examination are described in greater detail than in the first edition. The essentials of the diagnosis are summarized in a few pages, illustrated by diagrams and references to the plates. This greater attention to methods of examination is considered necessary by the authors, who feel that because the diagnosis depends essentially upon roentgenologic methods, the ordinary physician is not sufficiently experienced in such methods and needs detailed descriptions of methods. The recent anatomical and physiological knowledge of the intestinal tract is also given in greater detail. This second edition amplifies and revises in the light of later knowledge and experience the clinical studies upon which the first one was used. The basis principles stand however. The widespread appreciation of the book is responsible for this new edition. The publication of the first did much to stimulate interest in the study of intestinal tuberculosis, and the methods of diagnosis and treatment which it described have been chiefly responsible for the lifting of intestinal tuberculosis out of the realm of hopeless diseases into that of remedial affections. It was, therefore, primarily responsible for this marked change of attitude toward intestinal tuberculosis, which was almost universally formerly regarded as one of the hopeless sequelae of pulmonary tuberculosis. The frequency with which pulmonary tuberculosis is complicated by intestinal tuberculosis is well known to pathologists. It occurred to the authors that this complication might not always be a terminal condition, but might occur early enough in the course of the pulmonary infection to diminish greatly the chances of recovery from the lung lesion. The difficulty of diagnosis of the intestinal infection explains why for so many years the intestinal involvement has received so little attention from students of tuberculosis. The methods of diagnosis described in this book have led to a radical change in the point of view. Out of 5,542 patients examined roentgenologically for intestinal tuberculosis, 1,465 were found to be suffering from it. The material of the book is arranged as follows: Chapter I, The History of Intestinal Tuberculosis; II, The Anatomy of the Intestines; III, The Normal Physiology of Intestinal Movement; IV, V, VI, and VII, Pathological Anatomy of Intestinal Tuberculosis; VIII, Pathological Physiology of Movement; IX, Etiology of Intestinal Tuberculosis; X, Experimental Intestinal Tuberculosis; XI, Importance and Frequency of Secondary Intestinal Tuberculosis; XII, Site of the Lesions in Intestinal Tuberculosis; XIII, Primary and Secondary Intestinal Tuberculosis; XIV and XV, Clinical Symptoms of Intestinal Tuberculosis; XVI, Clinical Examinations of Intestinal Tuberculosis;

XVII, Relation of the Symptoms of Intestinal Tuberculosis to the Site of the Lesion; XVIII, The Abdominal Examination in Intestinal Tuberculosis; XIX, The Pulmonary Condition in Secondary Intestinal Tuberculosis; XX, XXI, XXII, and XXIII, Diagnosis of Intestinal Tuberculosis; XXIV, Complications of Intestinal Tuberculosis; XXV, Prognosis; XXVI, Prophylaxis, XXVII, Treatment; XXVIII, Conclusions and Summary. Roentgen-ray methods of diagnosis of first importance in intestinal tuberculosis are discussed in Chapters XXII and XXIII. Of all the complications of pulmonary tuberculosis, intestinal infection is the most frequent. A knowledge of intestinal tuberculosis is therefore essential for any physician who attempts to treat pulmonary tuberculosis. Until the roentgen-ray diagnosis was perfected, no one was able to state when in the course of a pulmonary tuberculosis, intestinal tuberculosis began, for it may be present for a long time without giving rise to symptoms. If it were only a terminal infection arising when all hope of recovery has vanished, its importance would be much less than it is today, since we know that intestinal infection may complicate very early cases, and is much more common among the moderately advanced, and very frequent in the advanced and terminal stages of pulmonary tuberculosis. It is for these reasons that this book is so important for the practitioner who treats cases of tuberculosis. Hypermotility with filling-defects indicates an ulcerative condition of the bowel, which in the presence of pulmonary tuberculosis is practically always of a tuberculous nature. The absence of hypermotility and filling-defects excludes for practical purposes the presence of tuberculous colitis. Digestive disturbances in the patient with pulmonary tuberculosis are always suspicious. It is now possible, by using the author's methods to decide whether these are functional or due to organic disease in the gastro-intestinal tract. To every physician who treats cases of pulmonary tuberculosis, this book is a necessary part of his armamentarium.

Edward Jenner and the Discovery of Smallpox Vaccination. By Louis H. Roddis, Lieutenant Commander, Medical Corps, United States Navy. Reprinted from The Military Surgeon, Vols. 65 and 66. 155 pages, 11 illustrations. George Banta Publishing Company, Menasha, Wisconsin, 1930. Price in cloth, $1.00.

This little volume is a well-written and interesting history of smallpox inoculation and vaccination, and particularly of Edward Jenner and the great part he played in the establishment of the knowledge of protection against smallpox. The historical knowledge of this disease up to the time of Jenner is first briefly sketched, and this is followed by a detailed history of inoculation as a preventive method, giving of course, due mention to Lady Mary Wortley Montague and the part played by her in the introduction of this method of prevention into England. Boylston, the first advocate of inoculation in North America, and Benjamin Franklin's "Some Account of the Success of Inoculation for the Smallpox in England and America," published in 1754, are given full credit for their share in spreading the use of this method on this side of the Atlantic. Chapter IV then takes up the life of Edward Jenner, his birth and education, and association and friendship with the Hunters. In 1771 Jenner returned to Gloucestershire to begin practice as a country doctor. He was essentially a country bred man, fond of country people and country life. Upon this choice of country practice as against practice in London, the most significant achievement of Jenner's scientific life depended. The observations which led to the discovery of smallpox vaccination could only have been made in a rural locality where dairying was carried on. Had Jenner remained in London at Hunter's suggestion, this chance would in all probability have been lost, and vaccination have remained undiscovered. An interesting picture is given of Jenner's life in Gloucestershire, his interest in natural history and music, his excursions into the realm of poetry, his domestic and professional life, etc., are all sketched in an entertaining and lively manner. Then comes the story of cowpox and Benjamin Jesty, the Dorset farmer, who first vaccinated with cowpox material. His wife was the first person in England known to have been in-

tentionally vaccinated with cowpox. Jenner's claims to distinction rest upon the fact that he took the countryside tradition of farmers and dairymaids, which other medical men ignored or scoffed at, studied the matter for nearly twenty-five years, experimented, observed, and recorded his findings, overcame all antagonism and opposition, and eventually succeeded in making of the countryside tradition a practical and usable medical procedure. Upon this fact his fame is firmly fixed for all time. The remainder of the book is taken up with the story of the spread of vaccination throughout the world, and of the last years and death of Jenner. This little volume gives a remarkably full account of Jenner's life and work; told in an interesting and lively manner, it holds the reader's attention from beginning to end. It is a chronicle of one of the greatest achievements of medicine, the work of a country practitioner, a never-to-be-forgotten fact. We recommend this little book to all of those who have an interest in the history of the development of medicine.

History of Haitian Medicine. By ROBERT P. PARSONS, Lieutenant-Commander, M.C., U.S.N. With a Foreword by EDWARD R. STITT, Rear Admiral, M.C., U.S.N. 196 pages, 21 illustration, and a folding map of Haiti. Reprinted with additions and corrections from Annals of Medical History, 1929. Paul B. Hoeber, Inc., New York, 1930. Price in cloth, $2.25 net.

This history was written in its original form in January, 1929, and appeared in that form in the May number, 1929, of the Annals of Medical History. Its publication aroused much interest, and this, with the recent prominent position of Haiti in the public eye, led to its publication in this form. Haitian history is a tale of turbulence, warfare and bloodshed, of intrigue and political factions, of comic opera revolutions, and of thinly-veneered civilization. Scratch its surface and one finds beneath it the savagery of Central Africa and the superstitious horrors of voodooism. The tom-tom still reverberates in the outlying mountainous recesses; and the Haitian blacks still celebrate the indecent orgiastic rites of their degenerate and primitive religion. Perhaps nowhere else in the world do the extremes of savagery and civilization meet as they do upon this island. Corresponding to the ignorance and illiteracy of the native population is their physical condition. Parsons describes the island as having been a veritable hotbed of diseases from the ravages of which some three million people in Haiti suffered. Almost every one of the rural population has had malaria, yaws, and intestinal parasites. Yaws, in particular, has been the physical curse of Haiti—first cousin to European syphilis, if not the same disease modified by age incidence, environment, and racial differences. For these diseases, until recently, there was no medical relief available. Up to ten years ago the mass of the Haitian people, to the number of three millions, was universally diseased, ill, crippled and weakened, helpless and hopelessly resigned to their lot. Parsons traces the thread of medical history; it falls logically into three principal periods: the French colonial period during the 17th and 18th centuries; the independent period from 1804-1915; and the period of American occupation since 1915. During the French colonial period there was little progress in Haitian medicine. The French physicians practiced among the classes of citizens who could afford to pay, or superintended in a very superficial way the medical treatment of the slaves. During the independent period the development of medicine was pathetically slow and interrupted by the numerous revolutions and successions of rulers. Particularly pathetic were the attempts to develop medical schools and hospitals. Among the influences for good was the American physician Lowell, who practiced medicine in the island from 1833-1845. Not until about 1890 was real progress made in the development of the medical school, and there began to be a scientific spirit in the practice of medicine and a scientific outlook on medical study. In this renaissance the leading spirit was Dr. Léon Audain. In the period from 1900 to 1910 original papers from Haiti appeared in French medical literature; a medical journal, "La Lanterne Médicale" was published for two years, and records of health conditions were made. From 1910-1915 there were seven different presidents in office; each suc-

ceeding one found the country sinking further down toward anarchy. Naturally the medical profession, medical school, and hospitals shared in this down-hill course; and when the Americans came in 1915, conditions were desperate and most deplorable. The sanitary problems confronting us were the greatest of all. Particularly was the yaws situation the great medical problem of the land. This was, however, not clearly realized until the arrival of Dr. Paul W. Wilson in 1922. The story of what the American occupation has done medically for Haiti is a wonderful one, and the book is worth reading for this story alone. Nevertheless, the final chapter on Haitian doctors leaves one pessimestic and apprehensive as to the final outcome of the contact of two cultures so diverse and so intrinsically opposite as the American and the Haitian.

College News Notes

Dr. Leo V. Schneider (Fellow) has resigned as Resident Physician at the State Sanatorium of Maryland, and accepted an appointment as Health Examiner for the Playground Athletic League of Baltimore, Maryland. His present residence is 3716 Springdale Avenue, Baltimore.

In the September Issue of the American Review of Tuberculosis Dr. Schneider contributed an article on "Primary Aspergillosis of the Lungs."

At the twenty-fourth annual meeting of the Seventh District Branch of the Medical Society of the State of New York, held at Keuka College, Penn Yan, N. Y., September 25, the following Fellows participated:

Dr. George L. Eckel, Buffalo (by invitation), "Anterior Poliomyelitis":

Dr. Wardner D. Ayer, Syracuse, discussion of the above paper;

Dr. James E. Talley, Philadelphia (by invitation), "Care of the Heart in Certain Infections";

Dr. John J. Finigan, Rochester, discussion of the above paper.

Dr. C. Harvey Jewett (Fellow), Clifton Springs, is the First Vice President, and Dr. John A. Lichty (Fellow), Clifton Springs, is the Secretary of the above society.

Dr. John A. Lanford (Fellow), Assistant Professor of Bacteriology and Pathology at the Tulane University of Louisiana School of Medicine, was guest of honor on the clinical program of the Northwest District (Alabama) Medical Society, October 3-4.

Dr. Robert S. Berghoff (Fellow), Chicago, addressed the McLean County (Ill.) Medical Society, September 9, on "Syphilis of the Heart."

Dr. Elliott P. Joslin (Fellow), Boston, delivered a paper on "Symptomatology and Treatment of Diabetes," October 7, at the meeting of the First District Branch (N. Y.) Medical Society's meeting in New York City.

Dr. James B. McElroy (Fellow), Memphis, spoke on "Ascites" at the Tri-County Medical Society of Tennessee, September 18.

Lieut. Col. William S. Shields (Fellow), M. C., U. S. Army, has been transferred from Fort Sam Houston, Texas, to the Fitzsimons General Hospital, Denver.

Dr. Laurence R. DeBuys (Fellow), New Orleans, is President-Elect of the American Pediatric Society.

Dr. Edwin C. Ernst (Fellow), St. Louis, President of the Radiological Research Institute, recently announced the incorporation of the Institute. Among their projectives is the production of x-ray tubes of a power now unavailable, in order that deeper penetration and faster action may be obtained. "Other objects of the society are cheaper radium, American control of its own radium supply, establishment of a central radiological research laboratory, fostering pure radiological research in colleges, co-operating with the National Institute of Health created by Congress, and establishment of an advisory board of fifty scientists to extend the practical application of x-ray research to all walks of life."

Dr. William S. Thayer (Fellow), Baltimore, was one of the invited guests to address the 61st annual session of the Medical Society of Virginia at Norfolk, October 21-23.

Other Fellows of the College who appeared on the program were:

Dr. Robert Finley Gayle, Richmond—"The Management of the Psychoneurotic";

Dr. David C. Wilson, University—"The Care and Prognosis of Extra-Mural Epileptics."

Dr. James W. Hunter, Jr. (Fellow), Norfolk, was host to members of the Virginia Roentgen Ray Society at a luncheon during the annual session of the Medical Society of Virginia.

Dr. Walter E. Vest (Fellow), Huntington, W. Va., President of the Alumni Association of the Medical College of Virginia, acted as Chairman of the Annual Alumni Luncheon, also during the meeting of the Medical Society of Virginia.

At the opening Convocation of the Medical College of Virginia, on September 17, Dr. Vest made an address on "Student Obligations."

Dr. W. A. Bloedorn (Fellow), Washington, D. C., addressed the London County (Va.) Medical Society, September 9, on "New Cardiac Aspects and New Cardiac Therapeusis."

Dr. F. C. Rinker (Fellow), Norfolk, Va., is Secretary of the Second District (Va.) Medical Society.

Dr. C. L. Harrell (Fellow), Norfolk, Va., presented a paper before the quarterly meeting of the Southside Virginia Medical Association, September 9.

Dr. Noble Wiley Jones (Fellow), Portland, Oregon, with Dr. Dorwin L. Palmer, is the author of an article entitled "Observations Upon Chronic Cholecystitis. With Special Reference to Motor Disturbances of the Gastro-Intestinal Tract in Relation to Preoperative and Postoperative Symptoms," appearing in the October Issue of the American Journal of The Medical Sciences.

Dr. I. Seth Hirsch (Fellow), New York, N. Y., Dr. Laurence H. Mayers (Fellow), Chicago, Ill., and Dr. Albert Soiland (Fellow), Los Angeles, Calif., are authors of the following papers or reports in the October Issue of Radiology, respectively: "Urography By Uroselectan," "A Concept of Arthritis" and "The Annual Meeting" (Radiological Society of North America).

Dr. Harold I. Reynolds (Fellow), Athens, Ga., and Dr. Trimble Johnson (Fellow), Atlanta, Ga., are authors of "Acute Poliomyelitis" and "Belladonna in Abdominal Diagnosis and Treatment," appearing in the September Issue of the Journal of the Medical Association of Georgia.

Dr. Stewart R. Roberts (Fellow), Atlanta, Ga., addressed the Ninth District Medical Society of Georgia at their September meeting on "Hypertension."

Dr. Harold I. Reynolds (Fellow), Athens, Ga., is President of the Eighth District Medical Society of Georgia.

Dr. Frank Garm Norbury (Fellow), Jacksonville, Ill., addressed the Morgan County (Illinois) Medical Society, September 11, on "Medical Observations Abroad."

Dr. Felix J. Underwood (Fellow), State Health Commissioner of Mississippi, addressed the Indiana State Board of Health at Fort Wayne, September 22-24, on "Results Accomplished by Full-Time County Health Departments."

Dr. Colonel B. Burr (Fellow), Flint, Mich., was the recipient of a complimentary dinner at Benton Harbor, Mich., by the Officers and Council of the Michigan State Medical Society on September 16.

At the meeting of the Second Councilor District Medical Society of Ohio, held at Dayton, September 24-26, the following Fellows of the College delivered the addresses indicated:

Dr. Stewart R. Roberts, Atlanta, Ga.—"Essential Hypertension, Well Established," "Hyperthyroidism with Accent on the Thyroid Heart Previous to Operation" "The Nervous Heart Without Organic Heart Disease Particularly if Vague Pains in the Left Precordium Are Present" "Agranulocytosis: Clinical Onset, Symptoms, Treatment," "Failing Heart and Its Realization" and "The

Heart and Circulatory Complications of Pregnancy."

Dr. Walter C. Alvarez, Rochester Minn. —"Diagnosis of Gastro-Intestinal Disease" and "Treatment of Organic and Functional (Digestive) Disease."

Dr. Ralph Pemberton (Fellow), Philadelphia, Pa., addressed the Northwestern Ohio Medical Society at Toledo, October 27, on "Arthritis."

Dr. Chester W. Waggoner (Fellow), Toledo, Ohio, President of the Ohio State Medical Association, addressed the same organization on "The Importance of the Practice of Medicine to a Community."

Dr. Frank Norman Wilson (Fellow), Ann Arbor, Mich., delivered an address entitled "Cardiac Weakness and Cardiac Failure" at the Annual Mercy Day at the Mercy Hospital, Pittsburgh, Pa., September 24.

Dr. Henry M. Ray (Fellow), Pittsburgh, Pa., spoke on "Clinical Significance of Spinal Fluid Examination, with Special Reference to Neurosyphilis" before the South Hills Branch of the Allegheny County Medical Society, September 18.

Dr. James C. Naurison (Fellow), Springfield, Mass., addressed the Windham County Medical Society (Vermont), recently, on "Diseases of the Heart."

Dr. Winthrop Adams (Fellow), who has been Medical Director of the United States Veterans' Bureau, has been assigned, at his own request, as Medical Officer in Charge of the Veterans' Neuropsychiatric Hospital at Bedford, Mass.

Dr. Henry I. Kloop (Fellow), Allentown, Pa., Superintendent of the Allentown State Hospital, delivered the Annual Report before the Homeopathic Medical Society of the State of Pennsylvania at Harrisburg on September 25.

Gifts of the following reprints to the College Library of publications by members are duly acknowledged as follows:

Dr. Donald L. Hamilton (Fellow), Sayre, Pa.,
Reprint—"Aneurysm of Anterior Cerebral Artery"

Dr. I. S. Kahn (Fellow), San Antonio, Texas:
3 Reprints—"Bronchial Asthma"
"The Intravenous Use of Epinephrin in Severe Bronchial Asthma"
"Tree Pollen Hay Fever and Asthma in the South"

Dr. Edgar F. Kiser (Associate), Indianapolis, Ind.:
2 Reprints—"Bronchomycosis"
"Pleural Effusion Associated with Congestive Heart Failure Localized in an Interlobar Space"

Dr. Carl V. Fischer (Fellow), Philadelphia, Pa.:
Reprint—"A Survey of the Progress in Internal Medicine, 1929"

Dr. G. Morris Golden (Fellow), Philadelphia, was the Chairman of the Section on Clinical Medicine and Pediatrics at the Sixty-seventh Session of the Homeopathic Medical Society of the State of Pennsylvania, held at Harrisburg, September 25-27.

Dr. Francis M. Pottenger (Fellow), Monrovia, Calif., attended the meeting of the Canadian Tuberculosis Association at Ninette, Manitoba, August 23, where he delivered an address on the subject of "The Relationship of the Vegetative Nervous System to Symptoms of Pulmonary Tuberculosis." About fifty tuberculosis workers were guests at this meeting.

Dr. Carl V. Vischer (Fellow), Philadelphia, read a paper, "Modern Advances in General Therapeutics," before the Homeopathic Medical Society of the State of Pennsylvania at its Sixty-seventh Session at Harrisburg, September 25.

Dr. E. W. Anderson (Associate), formerly of the Mayo Clinic, has recently become associated with the Hitchcock Clinic of Han-

over, N. H., and is an instructor in medicine in the Dartmouth Medical School.

At the Minneapolis meeting of the Inter-State Postgraduate Medical Association of North America, held October 20-24, 1930, the following Fellows of the American College of Physicians took part as indicated below:

Dr. Henry A. Christian, Boston, Mass.—A Medical Diagnostic Clinic and an address, "Clinical Types of Nephritis";

Dr. Harlow Brooks, New York, N. Y.—A Medical Diagnostic Clinic and an address, "The Periodical Physical Examination";

Dr. Elliott P. Joslin, Boston, Mass.—A Medical Diagnosis Clinic and an address, "Unclassified Glycosurias—Their Significance and Outcome";

Dr. Fritz B. Talbot, Boston, Mass.—A Pediatric Diagnostic Clinic and an address, "The Dietary Treatment of Epilepsy in Children";

Dr. William A. White, Washington, D. C.—An address, "Psychoses of Different Age Periods";

Dr. Emanuel Libman, New York, N. Y.—A Medical Diagnostic Clinic and an address, "Coronary Thrombosis and its Sequelae";

Dr. Charles A. Elliott, Chicago, Ill.—A Medical Diagnostic Clinic and an address, "Late Results of Thyroidectomy for Hyperthyroidism";

Dr. George E. Brown, Rochester, Minn.—A Diagnostic Clinic;

Dr. John H. Musser, New Orleans, La.—A Medical Diagnostic Clinic and an address, "Anemias Simulating Pernicious Anemia";

Dr. Elsworth S. Smith, St. Louis, Mo.—An address, "The Treatment of Essential Hypertension";

Dr. David P. Barr, St. Louis, Mo.—A Medical Diagnostic Clinic and an address, "The Significance of Jaundice";

Dr. Leonard G. Rowntree, Rochester, Minn.—A Medical Diagnostic Clinic and an address, "Cirrhosis of the Liver";

Dr. Henry S. Plummer, Rochester, Minn.—A Medical Diagnostic Clinic and an address, "Cause of the Specific Phenomena of Exophthalmic Goiter";

Dr. Stewart R. Roberts, Atlanta, Ga.—An address, "The Value of Tests for Liver Function";

Dr. Andrew C. Ivy, Chicago, Ill.—An address, "Observation on the Etiology of Gall Stones."

At a meeting of the newly appointed State Board of Health of Florida, held in the Governor's office in Tallahassee, October 25, Dr. H. Mason Smith (Fellow), Tampa, was elected President of the Board.

Dr. Grayson E. Tarkington (Fellow), Hot Springs, Ark., is the author of an article on "Encephalography," appearing in the August issue of the Hospital Bulletin of the Levi Memorial Hospital.

Dr. Harold Swanberg (Fellow), Quincy, Ill., recently contributed his publication "Radium Therapy in Uterine Malignancy" to the College Library of publications by members.

At the eighty-third semi-annual meeting of the Southern California Medical Association at Long Beach, October 31—November 1, the following Fellows of the College gave addresses as indicated:

Dr. Noel F. Shambaugh, Long Beach:
"The Dietary Factor in Kidney Disease"

Dr. Paul B. Roen, Los Angeles:
"Senility—Cause and Prevention"

Dr. Arthur L. Bloomfield, San Francisco:
"Indications for Use of Special Tests by the Practitioner"

Dr. Fred B. Clarke, Long Beach:
"Chronic Meningococcic Septicemia"

Dr. Edward W. Hayes (Fellow), Monrovia, and Dr. John Dwight Davis (Fellow), Los Angeles, addressed the Los Angeles Trudeau Society, October 28, on "The Practical Application of the Recent Classification of Tuberculosis in Children" and "Pathologic Changes of Lymph Nodes in Experimental Tuberculosis," respectively.

Dr. Joseph A. Capps (Fellow), Chicago, used as the subject of his Presidential ad-

dress before the Chicago Pathological Society, October 13, "Pathogenesis of Cardiac Pain."

Dr. Alexander A. Goldsmith (Fellow), Chicago, addressed the Tri-County (Ill.) Medical Society, October 13, on "Chronic Colitis."

Dr. Albert Austin Pearre (Fellow), Frederick, Md., addressed the semi-annual meeting of the Medical and Chirurgical Faculty of Maryland at Westminster, October 22, on "Symptomatology of Hypothyroidism in the Adult."

Dr. Philip S. Hench (Fellow), Rochester, Minn., addressed the joint meeting of the Tenth Councilor District Medical Society and the Allegheny County (Pa.) Medical Society, October 21, on "Clinical Consideration of Chronic Arthritis" and "Recent Progress in Study and Treatment of Rheumatic Diseases."

At the annual meeting of the Oregon State Medical Society, held at Portland, Dr. John H. Fitzgibbon (Fellow), Portland, was elected a Vice President.

Dr. John Eiman (Fellow) and Dr. Harold W. Jones (Fellow), both of Philadelphia, were speakers at a symposium on the blood diseases, at the October 8 meeting of the Philadelphia County Medical Society.

Dr. William Egbert Robertson (Fellow), Philadelphia, delivered an address on "Discussion of the Principles Presented and their Relation to General Medicine" before the Philadelphia County Medical Society, October 22, which meeting was devoted to a discussion of "Recent Applications of the Fundamental Sciences to Certain Medical Problems."

Dr. Samuel J. Goldberg (Associate), Philadelphia, addressed the West End (Philadelphia) Medical Society, October 15, on bronchitis.

The Norfolk County Medical Society was addressed on October 20 by Dr. Walter B. Martin (Fellow), Norfolk, on "The Value of Iron in the Treatment of the Anemias."

Dr. Otho A. Fiedler (Fellow), Sheboygan, Wis., was made President-Elect at the annual meeting of the State Medical Society of Wisconsin on September 11.

The thirtieth annual meeting of the Tenth District Medical Society, held at Eau Claire, Wis., was addressed by Dr. Francis D. Murphy (Fellow), on "Diabetes: Its Complications and Its Management."

Dr. Francis Eugene Senear (Fellow), Chicago, addressed the Medical Society of Milwaukee County, Wisconsin, October 10. His subject was, "Significance of Pruritus in Medicine."

Dr. James Stuart Pritchard (Fellow), Battle Creek, journeyed to Newark, Ohio, October 2, in his monoplane to address the Eighth District Ohio Medical Society on "Significance of the Cough as a Symptom."

Dr. Oliver T. Osborne (Fellow), New Haven, Conn., is the author of an article entitled, "Thyroid Gland," syndicated by the Gorgas Memorial Institute throughout the United States on October 11.

Dr. Osborne is also author of an article on "Medical Education," which appeared in the Medical Journal and Record, October 1. Dr. Osborne, furthermore, is author of several editorials which have appeared in recent issues of medical journals.

Dr. Sinclair Luton (Fellow) read a paper on "Recent Advances in the Study of Heart Diseases" before the Southwest Missouri Medical Society, Springfield, Missouri, November 6.

Acknowledgment is made of the receipt of the following reprints, which have been properly indexed and added to the College Library of publications by members:

Dr. Samuel Goldberg (Associate), Philadelphia, Pa.:

1 Reprint—"Mesentoric Embolism in a Haemophiliac"

Dr. Leo V. Schneider (Fellow), Baltimore, Md.:

5 Reprints—"Laryngeal Tuberculosis"
"Undulant Fever of the Pseudotuberculous Type and Pulmonary Tuberculosis"
"Bilateral Pleural Effusion Inflammatory Type Following Pneumonia"
"Tuberculosis and Malignant Neoplasia"
Primary Aspergillosis of the Lungs"

Dr. James Gurney Taylor (Fellow), Milwaukee, Wis., was a recent visitor to the College headquarters in Philadelphia.

Dr. Taylor has been elected a member of the National Board of Medical Examiners.

Dr. M. M. Canavan (Fellow), Curator of the Warren Anatomical Museum, Harvard University Medical School, has been granted leave of absence for three months, November 1, 1930, to February 1, 1931, for unofficial observations on medical conditions in Japan.

Dr. Henry Wallace (Fellow), New York, N. Y., addressed the annual meeting of the Piscataquis County (Maine) Medical Society at Deer Island on Moosehead Lake, recently, concerning the all around work of the general practitioner far from the large centers, and made a plea for the return of the general practitioner in general.

Dr. Clyde L. Cummer (Fellow), Cleveland, Ohio, was elected to membership in the American Dermatological Association at the recent annual meeting in Cleveland.

Dr. V. C. Rowland (Fellow), Cleveland, Ohio, is President of the Academy of Medicine of Cleveland.

The following list of reprints, of which Dr. Henry J. John (Fellow), Cleveland, Ohio, is author, is duly acknowledged:

"The Use of Intravenous Glucose in Diabetic Patients"
"The Importance of Early Diagnosis of Diabetes"
"Diabetic Coma"
"Diabetes"
"Diabetes"
"A Study of the Relation of the Blood Sugar in Plasma to that in the Corpuscles in Normal and Diabetic Individuals"
"Problems in Diabetes"

Dr. R. E. Loucks (Fellow), Detroit, Michigan, is author of an article entitled, "Ten Years' Results with Radium in the Treatment of Toxic Goiter," published in the American Journal of Roentgenology and Radium Therapy.

Dr. Howard S. Brasted (Fellow), Hornell, N. Y., was recently appointed Examining Physician for the Civil Service Commission of Hornell.

Dr. H. Lisser (Fellow and Governor for northern California is President of the California Academy of Medicine, a past President and a Councillor of the Association for the Study of Internal Secretions, and First Vice President of the San Francisco County Medical Society.

Dr. Lisser is a contributor to the Biedl Festschrift-Endokrinologie 1929, Volume 5, Pages 138-170: article entitled, "The Uniglandular Origin of Pluriglandular Syndromes." He is author of "A Further and Final Report on a Case of Tetanea Parathyreopriva treated for a year with Parathyroid Extract (Collip) with Eventual Death and Autopsy (with H. Clare Shepardson, (M.D.), Endocrinology, September, 1929, Volume 13, Page 427. Also, "Recent Endocrinology," California and Western Medicine, Volume 33, Page 545-550, August, 1930.

Lt. Col. Alexander T. Cooper (Fellow), M.C., U.S.A., retired September 29 as President of the Denver Sanatorium Association, being elected Honorary President.

Dr. Robert G. Douglas (Associate), Shreveport, La., addressed the Tri-County Medical Society of Arkansas, September 4, on "Diseases of the Colon."

At the Twentieth Annual Session of the American College of Surgeons at Philadelphia, October 17-17, the following Fellows of the American College of Physicians participated, as indicated below:

Dr. Orlando H. Petty, Philadelphia—Ward Class of Diabetic Surgery.

Dr. George E. Pfahler, Philadelphia—Exhibit of Technique and Results of Irradiation Treatment of Cancer of the Mouth;; Diagnosis of Bone Tumors; Radiation in the Diagnosis and Treatment of Malignant Disease.

Dr. H. L. Bockus, Philadelphia—Gastrointestinal Diagnosis.

Dr. George Morris Piersol—Cardiorenal Disease in Relation to Operative Risks.

Dr. O. H. Perry Pepper, Philadelphia (with George P. Muller)—Exploratory Laparotomy in Face of Roentgenological Evidence of Pulmonary Metastasis.

Dr. Wilson A. Myers (Fellow), Kansas City, spoke before the Jackson County (Mo.) Medical Society, September 30, on "Spondylolisthesis with Special Reference to the Etiology and Pathology."

Dr. Leonard G. Rowntree (Fellow), Rochester, Minn., initiated a heart campaign sponsored by the Health Conservation Association of Kansas City, October 7, by an address on "Recent Advances in the Study of Heart Disease."

Dr. Cyrus C. Sturgis (Fellow), Professor of Medicine and Director of the Thomas Henry Simpson Memorial Institute for Medical Research of the University of Michigan Medical School, delivered the Middleton Goldsmith Lecture for 1930 of the New York Pathological Society at the New York Academy of Medicine on October 18, his subject being, "Recent Development in the Treatment of Pernicious Anemia and a Consideration of the Etiology of the Disease."

The program for the Third Annual Graduate Fortnight of the New York Academy of Medicine, October 20-21; featured medical and surgical aspects of acute bacterial infections. Among the speakers were:

Dr. Charles F. Martin (Master), Montreal—"Continued Education of the Practitioner";

Dr. E. E. Irons, (Fellow), Chicago—"Facts and Fancies Concerning Vaccines and Non-Specific Therapy.";

Dr. Emanuel Libman (Fellow), New Work—"Acute and Subacute Bacterial Endocarditis";

Dr. William W. Herrick (Fellow), New York—"Meningococcus Infections, Including Meningitis."

Dr. Hal M. Davison (Fellow), Atlanta, addressed the Seventh District Medical Association of South Carolina, September 11, on "Neurosis in Internal Medicine."

Dr. James Allison Hodges (Fellow), Richmond, addressed the Clinch Valley Medical Society, of Virginia, at its annual meeting, September 20, on clinical education.

Dr. Frederick G. Banting (Fellow), Toronto, discoverer of insulin, was again honored on September 16 when the new $800,000 Banting Institute of the University of Toronto was dedicated. Lord Moynihan, President of the Royal College of Surgeons of England, presided.

The new building replaces the old pathologic building of the University ,and will combine its activities with the General Hospital. It is said that the cost of the building was contributed by the Provincial Government, the University and the Banting Research Foundation, which raised funds by popular subscriptions.

Dr. Lyell C. Kinney (Fellow), San Diego, addressed the San Diego County (Calif.) Medical Society, October 14, on "The County Medical Society—A Business Organization."

Dr. James G. Carr (Fellow and Governor for northern Illinois), Chicago, (with Dr. William C. Danforth) addressed the McDonough County (Ill.) Medical Society, October 14, on "Management of Pregnancy Complicated by Heart Disease."

Dr. Harry M. Hedge (Fellow), Chicago, used as his subject "Modern Conceptions and Treatment of Syphilis" in a talk before the Rock Island County (Ill.) Medical Society, October 14.

Dr. I. S. Trostler (Fellow), Chicago, spoke on "Roentgenotherapy of Conditions Other Than Cancer" before the McLean County (Ill.) Medical Society at Bloomington on October 14.

During a two-day school for physicians, under the auspices of the Public Health Board of Evansville, Indiana, in early October, Dr. Herman M. Baker (Fellow), Evansville, was one of the speakers; his subject having been "Nontuberculous Diseases of the Lung."

Dr. Noel C. Womack (Fellow), Jackson, Miss., addressed the Issaquen-Sharkey-Warren Counties (Miss.) Medical Society, September 9, on "Intracranial Hemorrhage in Infants."

Among speakers at the Northeast Mississippi Thirteen County Medical Society at Corinth, September 16, were: Dr. James S. McLester (Fellow), Birmingham, who spoke on the anemias; and Dr. Felix J. Underwood (Fellow), Jackson, who spoke on hospitals, nurses and health.

At the twenty-seventh annual meeting of the Nevada State Medical Associaton at Reno, September 26-27, Dr. De Los Schuyler Pulford, Jr. (Assocate), Woodland, Calf., spoke on "Benzol Posoning: a Report of a Case Simulating Anemia and Hemorrhagic Purpura"; and Dr. Edward Matzger (Associate), San Francisco, Calif., spoke on "Seasonal Hay-Fever and Seasonal Asthma—a Preventable Disease."

"The Physician as Community Counselor" was the subject presented by Dr. James K. Hall (Fellow), Richmond, Va., at the Ninth District (N. C.) Medical Society on September 25.

Dr. John T. Quirk (Associate), Piqua, Ohio, addressed the Miami County Medical Society at Troy, Ohio, September 5, on "Diagnosis and Treatment of Pernicious Anemia."

Dr. Robert A. Knox (Fellow), Washington, Pa., spoke before the Washington County Medical Society, October 15, on "Hypertrophic Stenosis of the Pylorus."

Dr. Lester Hollander (Fellow), Pittsburgh, addressed the Fayette County (Pa.) Medical Society, October 2, on "Eczema and Ringworm."

At the Commencement Exercises of Union University, June, 1930, the degree of Doctor of Science was conferred on Dr. Hermon C. Gordinier (Fellow), Professor of Medicine at the Albany Medical College.

Dr. James M. Anders (Master) has been appointed Chairman of the Better Homes Committee of Philadelphia for the year 1930-1931 by Dr. Wilbur, Secretary of the Interior, Washington, D. C.

Dr. Willard C. Stoner (Fellow), Cleveland, Ohio, addressed The Union Medical Association of the Sixth Councilor District at Kent, Ohio, on October 8, on "The Importance of an Intensive Program in the Treatment of Chronic Arthritis and Rheumatic Manifestations," and on October 20 he addressed The American Protestant Hospital Association at New Orleans on "The Increasing Cost to the Patient of Medical and Hospital Care."

COLLEGE MEMBERS MEET IN WESTERN PENNSYLVANIA

On October 25, Dr. E. Bosworth McCready, Governor of the American College of Physicians for western Pennsylvania, along with Dr. Clement R. Jones, Treasurer of the College, arranged a sectional gathering of all of the Fellows and Associates residing in western Pennsylvania. A dinner was held at the Duquesne Club in Pittsburgh, with the following Fellows present: Dr. Syndey R. Miller, President, Baltimore, Md.; Dr. George Morris Piersol, Secretary General, Philadelphia; Dr. Clement R.

Jones, Treasurer, Dr. E. Bosworth McCready, Governor, Dr. J. M. Thorne, Dr. C. C. Hartman, Dr. J. H. Barach, Dr. F. A. Evans, Dr R. R. Snowden, Dr. George W. Grier, Dr Shaul George, Dr. Henry M. Ray, Dr. Lester Hollander, Dr. H. W. Weurthele, all of Pittsburgh; Dr. L. D. Sargent, Dr. R. A. Knox, Dr. G. W. Ramsey, all of Washington; Dr. C. C. Campman, of West Middlesex, Dr. H. B. Anderson, of Johnstown, Dr. G. H. Hess and Dr. E. B. Edie, of Uniontown; and Dr. W. G. Falconer, of Clearfield. In addition, the following Associates were present: Dr. E. M. Frost, Dr. H. A. Shaw, Dr. Max Weinberg, all of Pittsburgh; Dr. G. F. Stoney, of Erie; Dr. G. A. Ricketts, of Osceola Mills. Mr. E. R. Loveland, the Executive Secretary from Philadelphia, was also present, as were also eleven invited guests.

Governor McCready and Treasurer Jones made appropriate remarks concerning the activities of the College in western Pennsylvania. Mr. Loveland spoke briefly of the business organization and operation of the College. Secretary General Piersol spoke at length concerning the standards of the College with respect to admission and the work of the Committee on Credentials. President Miller acted as Toastmaster, giving at the end an inspiring address concerning the whole field of activity for the College and outlined the laudable objects the College should accomplish. The meeting contributed much to the enthusiasm and understanding of the members of the College, as well as promoted good fellowship generally. This was the second sectional gathering held during the past few months by members of the College; the previous one being the Fellows and Associates of the College in the State of North Carolina. The effects of these sectional gatherings are far-reaching and inspiring, and should be encouraged throughout all parts of the country.

THE COLLEGE LIBRARY

Have You Contributed?

Two years or more ago, the Board of Regents conceived the idea of establishing a library of books of which its members are the authors. The library, in a sense, is intended to be a Memorial Library to its members. A general medical library, other than one composed of publications by the members, would scarcely be justified in the College headquarters, both due to inadequate housing facilities and lack of availability to members. However, there are ample facilities for a library of all of the books that have been published by Fellows of the College, and such a library is of considerable value and great interest.

It is regretted that comparatively so few of the members have actually contributed their books. Reprints have been submitted in profusion, and are gratefully received, but a library of mere reprints does not approach in interest a library of books. Fellows of the American College of Physicians constitute a group of probably the most productive medical men of America. Books of which they are authors are not only numerous, but occupy a forefront position in American medical literature.

Your contributions should be sent to the Executive Secretary, Mr. E. R. Loveland, 133-135 S. 36th Street, Philadelphia, Pa., who will promptly acknowledge their receipt, both to you personally and in the columns of the Annals of Internal Medicine. They will then be properly indexed, both by title and author's name, and placed on the bookshelves in the reception room of the College.

Dr. Herbert W. Rathe (Associate), Waverley, Ia., "Coronary Disease with Special Reference to Acute Coronary Accidents, Their Recognition and Treatment"

Dr. Charles N. Hensel (Fellow), St. Paul, Minn., "Nonmyxedematous Hypothyroidism"

Dr. Moses Barron (Fellow), Minneapolis, "Treatment of Bright's Disease"

At the annual meeting of the Medical and Surgical Association of the Southwest at El Paso, Texas, November 6-8, the following Fellows were scheduled to deliver addresses indicated.

Dr. George R. Herrmann, New Orleans, illustrated lectures—"Diagnostic Criteria of Heart Disease" and "Treatment of Syphilitic Aortic Disease in the Last Stages";

Dr. Roy E. Thomas, Los Angeles, "Management of Lobar Pneumonia";

Dr. Walter C. Alvarez, Rochester, Minn., "Practical Points in Treatment of Gastro-Intestinal Disease";

Dr. LeRoy S. Peters, Albuquerque, "Cauterization of Adhesions—Jacobaeus—Unverricht Method".

Dr. Edward Matzger (Associate), San Francisco, addressed the San Francisco County Medical Society, August 12, on "Studies in Human Hypersensitiveness—Recent Advances".

Dr. James K. Fancher (Associate), Atlanta, Ga., addressed the Fulton County Medical Society, August 7, on "The Influence of Sodium Cacodylate on the Leukocyte Count".

At the 80th annual session of the Kentucky State Medical Association, held at Bowling Green, September 15-18, Dr. Oscar O. Miller (Fellow), Louisville, delivered an address on "Present-Day Conception of Pulmonary Tuberculosis in Infancy and Childhood".

Dr. Emmet F. Horine (Fellow), Louisville, delivered the oration in medicine on "Mechanism of the Heart Beat".

The annual meeting of the Southern Minnesota Medical Association, August 25, at Mankato, was addressed by the following members of the College:

Dr. Walter C. Alvarez (Fellow), Rochester, Minn., "The Art of Medicine"

At the eighth annual fall clinical conference of the Kansas City Soutwest Clinical Society, held in Kansas City, October 6-10, Dr. Leonard G. Rowntree (Fellow), Rochester, Minn., and Dr. Ralph C. Matson (Fellow), Portland, Oregon, were guests speakers.

Dr. Oliver P. Kimball (Fellow), Cleveland, addressed the Portland City and County Medical Society at Portland, Ore., July 16, on "Relation of Thyroid Disease to Mental Deficiency".

Dr. Jack Witherspoon (Fellow), Nashville, Tenn., addressed the Northeastern Division of the Alabama State Medical Association, June 24, on duodenal ulcer.

Dr. Herman N. Bundesen (Fellow), Chicago, was one of the speakers at a symposium on crime detection, August 27-30, conducted by the Scientific Crime Detection Laboratory and Northwestern University.

Dr. Louis M. Warfield (Fellow), Milwaukee, addressed the 110th annual meeting of the Michigan State Medical Society at Benton Harbor, September 15-17, on "Tachycardia".

At the meeting of the Eastern Oregon District Medical Society, August 27, Dr. John H. Fitzgibbon (Fellow), Portland, delivered a paper on "Occlusion of the "Fallopian Tubes", and Dr. Marr Bisaillon (Fellow), also of Portland, gave a paper on "Pulmonary Tuberculosis".

Dr. Frank Howard Richardson (Fellow), Black Mountain, N. C., and Dr. Horton R. Casparis (Fellow), Nashville, Tenn., addressed the Spartanburg County Medical Society (South Carolina), July 28, on "Posture in Children" and "Causes of Infant Mortality During First Year of Life", respectively.

Dr. Aldred Scott Warthin (Master) Ann Arbor, Michigan, addressed the 36th annual meeting of the Utah State Medical Association at Salt Lake City, September 9, on "The Newer Therapeutic Attack on Cancer".

The same meeting was addressed by Dr. Andrew C. Ivy (Fellow), Chicago, on "Observation on the Cause of Gallstones"; by Dr. William Gerry Morgan (Fellow), Washington, D. C., on "Some Observations on Etiology"; and by Dr. William S. Thayer (Fellow), Baltimore.

At the annual meeting of the American Protestant Hospital Association at New Orleans, October 17-20, among the sched-

uled speakers appeared the following Fellows of the College:

Dr. John H. Musser, New Orleans, "Interns";

Dr. Willard C. Stoner, Cleveland, "The Increasing Cost of Medical and Hospital Care".

Dr. Christopher G. Parnall (Fellow), N. Y., was the guest of honor at the annual banquet.

Dr. Joseph G. Terrence (Associate), Brooklyn, N. Y., was recently elected to the Presidency of the Brooklyn Society of Internal Medicine.

Dr. Judson Daland (Fellow), Philadelphia, has just returned from visiting South America, where he was studying the diseases peculiar to that Continent.

Dr. Edgar Erskine Hume (Fellow), Major, Medical Corps, U. S. Army, who has been Medical Inspector of the Infantry School at Fort Benning, Georgia, was transferred to Boston on October 1. Dr. Hume was the recipient of the degree LL.D. from the University of Kentucky last June.

SOUTHERN MEDICAL ASSOCIATION MEETING

The Southern Medical Association held its twenty-fourth annual meeting at Louisville, Kentucky, November 11-14, 1930. Members of the American College of Physicians occupied one hundred and twenty-four distinct assignments. Among the more important, the following are mentioned:

Dr. Hugh S. Cumming (Fellow), Washington, as President;

Dr. Walter E. Vest (Fellow), Huntington; Dr. Morgan Smith (Fellow), Little Rock; Dr. William Gerry Morgan (Fellow), Washington; Dr. Sydney R. Miller (Fellow), Baltimore; Dr. W. McKim Marriott (Fellow), St. Louis; Dr. Lea A. Riely (Fellow), Oklahoma City; and Dr. Alfred L. Gray (Fellow), Richmond, as Councilors;

Dr. Stewart R. Roberts (Fellow), Atlanta; Dr. C. C. Bass (Fellow), New Orleans; and Dr. William R. Bathurst (Fellow), Little Rock, as members of the Board of Trustees.

Among those occupying offices on various sections are the following:

Section on Medicine—Dr. C. W. Dowden (Fellow), Louisville, Chairman
Dr. T. Z. Cason (Fellow), Jacksonville, Vice Chairman

Section on Pediatrics—Dr. H. Leslie Moore, Dallas, Chairman
Dr. Philip F. Barbour (Fellow), Louisville, Host

Section on Gastro-Enterology—Dr. G. W. F. Rembert (Fellow), Jackson, Chairman
Dr. Elmer B. Freeman (Fellow), Baltimore, Secretary
Dr. Charles G. Lucas (Fellow), Louisville, Host

Section on Neurology and Psychiatry—Dr. R. Finley Gayle, Jr. (Fellow), Richmond, Chairman
Dr. Charles S. Holbrook (Fellow), New Orleans, Vice Chairman
Dr. William E. Gardner (Fellow) and Dr. John J. Moren (Fellow), both of Louisville, Hosts

Section on Medical Education—Dr. Robert Wilson (Fellow), Charleston, Chairman
Dr. Russell H. Oppenheimer (Fellow), Atlanta, Vice Chairman
Dr. Kenneth M. Lynch (Fellow), Charleston, Secretary
Dr. John Walker Moore (Fellow) and Dr. Virgil E. Simpson (Fellow), both of Louisville, Hosts

Among Fellows of the College offering scientific exhibits were the following:

Dr. W. W. Duke (Fellow), Kansas City, Mo., offered a scientific exhibit showing various causes and effects of allergy, methods of study, methods of diagnosis and treatment, and methods of preparation of material for diagnosis and treatment.

Dr. Charles N. Kavanaugh (Fellow), Lexington, gave a scientific exhibit on Tularemia—color photographs of lesions, gross and microscopic.

Dr. Emmet F. Horine (Fellow), Louisville, moving pictures of the mechanism of cardiac action.

Dr. W. W. Anderson (Fellow), Atlanta, photographs of clinical conditions in children.

On the General Session, Dr. Emmet F. Horine (Fellow) gave the Presidential Address of Welcome in behalf of the Jefferson County Medical Society. Dr. Hugh S. Cumming (Fellow), Surgeon General of the U. S. Public Health Service and President of the Southern Medical Association, gave the annual Presidential Address on "Future Relations of the Profession to the Public." Dr. M. W. Ireland (Fellow), Surgeon General of the U. S. Army, gave the oration on surgery, "The Relation of Internal Medicine and Surgery." Dr. Alfred Stengel (Master) Professor of Medicine at the University of Pennsylvania School of Medicine, gave the oration on medicine, "Empiricism and Science in Medical Practice."

At the General Clinical Sessions, the following contributed, as indicated:

Dr. John J. Moren (Fellow), Louisville, "Post-Encephalitic Phenomena, Parkinsonian Type";

Dr. William E. Gardner (Fellow), Louisville, "Jamaica Ginger Paralysis";

Dr. Philip F. Barbour (Fellow), Louisville, "Anemia of the Newborn";

Dr. Oscar O. Miller (Fellow), Louisville, "New Methods in the Management of Chronic Tuberculosis";

Dr. Allen H. Bunce (Fellow), Atlanta, "Differential Diagnosis of Abdominal Conditions";

Dr. Stewart R. Roberts (Fellow), Atlanta, "The Heart in Pregnancy";

Dr. John H. Musser (Fellow), New Orleans, "The Blood in Disease".

In the Section on Medicine, the program was offered almost wholly by Fellows of the College. We list the following who offered papers, but omit the names of discussants:

Dr. C. W. Dowden (Fellow), Louisville, Chairman's Address;

Dr. Cyrus C. Sturgis (Fellow), Ann Arbor, "The Treatment of Pernicious Anemia";

Dr. J. E. Knighton (Fellow), Shreveport, "Melanomatosis with Case Report";

Dr. J. Heyward Gibbes (Fellow), Columbia, S. C., "The Results of Agglutination Tests for Undulant Fever";

Dr. W. W. Duke (Fellow), Kansas City, "New Aspects of Gastro-Intestinal Allergy";

Dr. C. H. Cocke (Fellow), Asheville, "The Healing of Tuberculosis."

To the Section on Pediatrics, the following contributed papers or clinics:

Dr. Philip F. Barbour (Fellow) and Dr. James W. Bruce (Associate), Louisville, a Clinic:

Dr. H. Leslie Moore (Fellow), Dallas, "A Clinical Observation in Nutritional Injuries";

Dr. Fritz B. Talbot (Fellow), Boston, "Endocrine Disturbances in Childhood";

Dr. Ray M. Balyeat (Fellow), Oklahoma City, "Manifestations of Allergy in Children";

Dr. C. C. McLean (Fellow), Birmingham, "Periodical Seasonal Incidence of Gastro-Intestinal Symptoms Complicating Respiratory Infections in Childhood";

Dr. W. McKim Marriott (Fellow), St. Louis, "Enteral and Parenteral Factors in the Causation of Diarrhea";

Dr. Carroll M. Pounders (Fellow), Oklahoma City, "Appendicitis in Children from the Pediatrist's Point of View".

In the Section on Gastro-Enterology, again members of the College contributed a large portion of the program:

Dr. G. W. F. Rembert (Fellow), Jackson, Chairman's Address on "Gastro-Enterology: An Important Phase in Diagnostic Procedure";

Dr. Walter C. Alvarez (Fellow), Rochester, "Some Practical Points in the Treatment of Gastro-Intestinal Diseases";

Dr. Daniel N. Silverman (Fellow), New Orleans, "Bacterial Forms of Dysentery in the South: A Clinical and Bacteriological Study";

Dr. Jack Witherspoon (Fellow), Nashville, "Spastic Constipation";

Dr. L. C. Sanders (Associate), Memphis, "Carcinoma of the Colon: A Plea for Early Diagnosis";

Dr. Julius Friedenwald (Fellow) and Dr. Theodore H. Morrison (Fellow), Baltimore, "Some Observations on the Secondary Gastric Disturbances Occurring in Pulmonary Tuberculosis";

Dr. Seale Harris (Fellow), Birmingham, "The Dietary Management of the Ulcer Patient Before and After Operation";

Dr. John B. Fitts (Fellow), Atlanta, "Cancer of the Stomach in the Southern Negro: A Study of Fifty Cases".

To the Section on Pathology, Dr. Aldred Scott Warthin (Master), Ann Arbor, delivered an illustrated paper on "The Pathology of Latent Syphilis."

To the Section on Neurology and Psychiatry, the following contributed papers:

Dr. R. Finley Gayle, Jr., (Fellow), Richmond, Chairman's Address, "The Relationship Between Neurology and General Medicine and Surgery";

Dr. Walter Freeman (Fellow), Washington, "Malaria Therapy in Private Practice".

To the Section on Radiology, Dr. W. P. Baker (Fellow), Atlanta, contributed a paper on "Observations Based Upon the Treatment of Six Hundred Cases with Deep X-Ray Therapy."

To the Section on Public Health, Dr. O. C. Wenger (Fellow) of the U. S. Public Health Service, Hot Springs National Park, contributed a paper on "The Incidence of Syphilis in the Negroes of the South."

To the program of the National Malaria Committee, Dr. Engene R. Whitmore (Fellow), Washington, contributed a paper on "Plasmochin in Malaria."

To the Section on Medical Education, the following contributed, as indicated:

Dr. Robert Wilson (Fellow), Charleston, Chairman's Address on "Aims and Methods in Education";

Dr. James S. McLester (Felow), Birmingham, "The Teaching of Therapeutics";

Dr. Charles T. Stone (Fellow), Galveston, "Levels of Nursing: The Practical Nurse, the Trained Nurse, the Specialized Nurse, and Their Relations to the Economics of Illness";

Dr. W. S. Leathers (Fellow), Nashville, "The Responsibility of the Medical School in the Education of the Nurse."

OBITUARY

Dr. William Burley Bowman (Fellow), Los Angeles, Calif., died, October 20, 1930, of heart disease.

Dr. Bowman was born at Martin's Ferry, Ohio, in 1885. He received his medical training at St. Louis University School of Medicine, from which he graduated in 1910. He went to Los Angeles soon after graduation, and established hospital connections as Attending Roentgenologist to the California Lutheran and St. Vincent's Hospitals and at the University of California Postgraduate Clinic. He early limited his efforts to X-Ray work, in which field he became one of the outstanding men in the community. His earnest endeavor in the field of Roentgenology and his efforts in the fields of constructive medicine made him widely known.

At the time of his death, he was attending Roentgenologist to the Santa Fé and Methodist Hospitals; Consulting Roentgenologist to the Children's and General Hospitals and to the Barlow Sanatorium. He was a member of the Alpha Kappa Kappa Fraternity, the Los Angeles County Medical Society, the American Roentgenological Society, the California State Medical Society, the Clinical and Pathological Society, the American Association of Military Roentgenologist and a Fellow of the American Medical Association. He had been a Fellow of the American College of Physicians since April 3, 1922. His sudden death was a shock to his friends and colleagues everywhere.

—Furnished by Egerton L. Crispin, M.D., F.A.C.P., Governor for Southern California.

Dr. Murrett Fauquier DeLorme (Fellow), Brooklyn, N. Y., died September 8, of heart disease; aged 61 years.

Dr. DeLorme was born at Sumter, North Carolina. He attended the University of Maryland, Department of Pharmacy, from which he received the degree of Ph.G. He then attended the Bellevue Medical College during the years 1896-1897; thence he transferred to the Long Island College Hospital from which he received the degree of Doctor of Medicine in 1900. At the Long Island College Hospital, Dr. DeLorme was Instructor in Pharmacy and Materia Medica from 1900 to 1903; from 1903 to 1906, Lecturer in Pharmacology; from 1907 to 1915, Assistant Professor in Materia Medica and Pharmacology, and since 1916, had been Clinical Professor of Medicine.

Dr. DeLorme numbered among his publications the following: "A Manual of Pharmacy for Physicians," in three editions, published by P. Blakiston's Sons and Co.; "A Syllabus of Materia Medica," published by J. C. Lindsay Co.; and "An Experiment in the Application of Diabetic Dietetics," published in the Journal of the American Medical Association.

He was a Fellow of the American Medical Association; a member of the Medical Society of the County of Kings; a member of the Medical Society of the State of New York; a member of the Associated Physicians of Long Island and a member of the Society of Internal Medicine of Brooklyn. He was among the original group who met at the Hotel Astor, New York, in 1915 to formulate plans for

the founding of the American Congress on Internal Medicine, but did not become a Fellow of the American College of Physicians until 1928. He was an active member of the College, enthusiastic about its policy and objects.

Dr. Herman C. Gordinier (Fellow), prominent physician, and a specialist on lung and heart disease, died last month at his home at 89 Fourth Street, Troy, New York. He had been ill for a long time. Dr. Gordinier was 66 years old. He was born in Troy, May 21, 1864, and always resided here, where he studied and built up his lucrative practice. He was educated in the public schools and was graduated from the Albany Medical College in 1886. Subsequently he took a course at the University of Prague in Austria.

For more than 40 years he was a Professor in the Albany Medical College, where he was noted for his thoroughness. He was one of the founders and a member of the Board of Trustees of the Samaritan Hospital, where he served as a physician and neurologist. He was also a physician at the Mary McClellan Hospital at Cambridge.

He was an instructor in physical diagnosis in the Albany Medical College from 1889 to 1895, after which he became a Professor of Anatomy and Physiology and finally Professor of Medicine. Dr. Gordinier received a number of honorary degrees, including Master of Arts from Williams College and Doctor of Science from Union College.

He was a member of numerous societies, including the Rensselaer County Medical Society, the New York State Medical Society and the American Medical Association. He was also an honorary member of the American Neurological Society, the American Physicians Society, the American Therapeutic Society, the New York Academy of Medicine and the American College of Physicians. For many years he held offices in all the organizations.

He was a member of the Troy Club, the Troy Country Club, the Troy Riding Club, Mount Zion Lodge, F. and A. M., and the Scottish Rite Societies. He was a Director of the Union National Bank.

Dr. Gordinier contributed a number of articles to medical books and magazines. During his early days he published a catalogue on "Flora and Fauna of Rensselaer County." He was the author of a number of books on nervous diseases.

Dr. Gordinier's death removes one of the city's noted citizens and one of the best physicians in this part of the country. He is survived by two daughters, Miss Hermione Gordinier and Mrs. George P. Ide, 2d; one son, Hermon C. Gordinier, all of this city, and a brother, Adam Gordinier of Schenectady.

The funeral was held Wednesday afternoon at 2:30 o'clock from St. John's Episcopal Church. Rev. Dr. Henry R. Freeman, rector emeritus of St. John's Church, officiated. Interment was in Oakwood Cemetery.

Mayor Burns paid the following tribute to Dr. Gordinier:

"The passing of Dr. Hermon C. Gordonier removes from our city one of its most distinguished native citi-

zens. As a physician, he was a leader, commanding the respect and admiration of his professional colleagues. As a man and a friend he was known to thousands, who had for him the utmost confidence and regard.

"During his years of professional life, Dr. Gordinier gave unceasingly and unselfishly if his time and talents to administer to those who needed him. Devotion to duty, and love for his fellow beings were his motives, rather than the idea of monetary reward in hundreds of cases where his patients could ill afford to pay. No personal sacrifice was too great if, because of it, someone benefited.

"As a professor of medicine at Albany Medical College he passed on to those entering the profession much of the knowledge which had placed his name in the fore in medical circles in the nation.

"Dr. Gordinier brought to his native city a high honor, for he was more than a loyal physician, and his fame extended far. As Mayor of the city which reflected his glory, I voice the regrets of its people at his death. Personally, I counted Dr. Gordinier as a friend, and to have been was an honor of which anyone can justly be proud.

"Dr. Gordinier will be missed and his place will be most difficult to fill. But those who mourn him will find solace in the knowing that he has gone on to the reward which he so well earned."